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AFTER THE DROUGHT A CLOUDBURST

THERE has been a good bit of speculation on what will happen if the college reservoir of postwar pharmacists reaches flood level after 1951, as expected. Growing apprehension appears in both the A. PH. A. resolution urging proper selection of students and the action taken at the October meeting of the Pharmaceutical Survey Committee.

The Survey director put the facts on the table: Evidence that total freshman enrollment this year will be over 6000. Total enrollment about 18,000 compared with around 8000 before the war. Prospects that in the years ahead colleges will be turning out double the number of graduates considered to be normal replacements.

What does this mean in terms of the profession and in terms of the level of professional service offered the public? The consensus of the Survey Committee was that it bodes no good.

The Survey is recommending that the AACP ask each college to adjust enrollments to avoid an oversupply of graduates after 1951 in the region it normally serves. Each state board is asked to maintain careful estimates of the need for licensed pharmacists in the state and to keep the colleges in its area informed. The Council on Pharmaceutical Education is asked, in re-accrediting a college, to attach particular importance to the question: What is the institution's policy on maintaining the size of student classes at a level consistent with teaching facilities and the capacity of the profession to absorb the graduates?

In the light of data reported by the Survey, this program appears sound; effective only if activated by the groups involved. It should gain the support of practicing pharmacists who take the long view, no matter how difficult it may be at the present moment to maintain adequate licensed staffs.

It seems to deserve this support even on the basis of present enrollments. We can expect graduates during the next four years to fill out war-depleted ranks. And there should be enough left over—upwards of 2000—to balance the numbers entering graduate study and to fill expanded opportunities in some fields. Against this background it becomes clear why the Survey group expresses concern now about continued excessive enrollments, for the graduates of 1952 will be applying for college entrance next fall.

We doubt that the profession can then continue to assimilate over twice the number of graduates normally needed in the past without getting a bad case of indigestion. With the shortage of educators and facilities, we doubt that the majority of colleges can maintain sufficiently high teaching standards. This offers no advantage to pharmacy, the graduate or the public.

A FOUNDATION FOR THE FUTURE

THE importance of a National Science Foundation to American communities and to pharmacy and medicine was again recognized by the A.PH.A. in a resolution adopted at the Milwaukee meeting. "Science" has become almost a fetish with the American public but it has not been easy to drive home the fact that applied research—the kind that makes the headlines—has far outstripped pure research.

After prolonged debate and delay Congress passed legislation for a National Science Foundation at the last session. President Truman reluctantly vetoed it. The nub of the controversy centers around administration of the Foundation, not its objectives. Our ASSOCIATION wisely directed the Council to study these differences and "to take such action as may be necessary" to help secure a Foundation.

The Foundation would recognize one of the most important facts of life in modern science: Fundamental research problems are apt to be so complex and expensive that they are over the heads of most universities and similar institutions. They do not get adequate support from industry because they lack foreseeable commercial value. The Foundation would encourage deep digging for basic scientific principles without too much concern about what the "practical" value may be. In its medical aspects this represents raw material from which applied research may fashion new weapons against disease.

The Foundation is also planned to encourage development of high-power scientific personnel through scholarships and fellowships, and would continue the national roster of scientific specialists that proved so valuable during the war.

The intellectual sources of Europe upon which we have borrowed heavily are bankrupt. It is to our own advantage here, as well as to other peoples, for the United States to pick up where Europe left off. It is within the broad interests of A. PH. A. members as citizens and pharmacists to ask the new Congress to give attention to reaching an acceptable compromise on legislation for the Science Foundation.

FORMULAS FOR FACIAL MASK

Sirs:

A few patrons have asked us to compound for them a good, stable, safe facial mask or mudpack. Do you have available such a formula?

Columbus, O. MRS. NELSON FARRAND

For information on facial masks and other cosmetic products we refer you to The Chemistry and Manufacture of Cosmetics, *by deNavarre (D. Van Nostrand Company, Inc., 250 4th Ave., New York, N. Y.), from which the following formulas are taken:*

Methyl cellulose, low viscosity	*10*
Sorbitol syrup	*5*
Kaolin	*3*
Water	*82*

Color, preservative and perfume.

Procedure: Add the methyl cellulose to boiling water which has previously been preserved. Let set 24 hours with occasional stirring. Next day add the paste made by rubbing down sorbitol with kaolin along with some water-soluble perfume like phenyl-ethyl alcohol or terpinol.

This mask dries in about 20 minutes after it is brushed on, and can be peeled off if desired. The continuity of the film will depend somewhat on the evenness of the preparation painted on.

Gelatin is also useful in formulating liquid face masks. A typical formula follows:

Sodium borate	*1*
Gelatin, type B	*2*
Karaya gum	*0.2*
Glycerin	*3*
Water	*93.8*

Color, preservative and perfume.

Procedure: Dissolve gelatin and glycerin in part of water previously preserved with butyl p-hydroxybenzoate; make a mucilage of karaya (as described earlier in the chapter), using preserved water. Mix the two solutions, add the borax and let set in open containers for several days. Gelatin must be buffered to prevent gel formations.

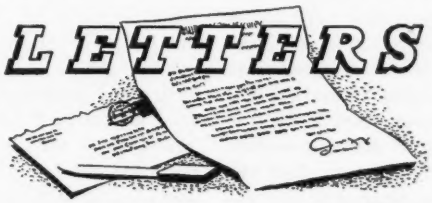
Note: Unless gelatin made from an alkaline precursor (type B) with an iso-electric point of 4.7 is used, a coascervate will form, and the resulting mixture throws out the gum and gelatin as a curd.

JOINS PROF. MEUSER IN WEST CHINA

Sirs:

You may be interested to learn that I came here from Chungking a week ago to join the pharmacy department of the West China Union University to work with Dr. Meuser, whom you know. As a professor I shall teach the practice of pharmacy, dispensing and direct some research work. Will you kindly change my address and have both editions of the JOURNAL sent here from now on?

Chengtu, West China S. Y. CHEN



PHARMACY IN INDIA

Sirs:

I acknowledge with many thanks the National Pharmacy Week material which you were good enough to send to me. It is interesting to see how you push the cause of pharmacy in America. We in India are far away from such a program since the profession of pharmacy is, relatively, in its childhood here.

Bombay, British India C. A. ROTHENHEIM

BACK IN THE STATES

Sirs:

Since leaving Panama I have not been a member of any branch of your ASSOCIATION. Recalling the fine contributions you have made to raising pharmaceutical standards, I am glad to enclose my dues for the next year.

Grants, N. M.
THOMAS E. CADY

A NOTE FROM JAPAN

Sirs:

I am happy to be able to write you for the first time. We are very satisfied with the U. S. military library in Tokyo but am sorry to say that we can't find the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION on the bookshelves.

We want to receive your splendid JOURNALS, both the *Practical Pharmacy* and *Scientific Editions* on exchange. I will send you our journals as soon as authorization from General Headquarters becomes effective.

M. HASHIZUME, Editor
Japan Pharmaceutical Association
Tokyo Imperial University
Tokyo, Japan

COMMENT FROM MEMBERS

Sirs:

Enclosed please find my check for annual dues and for a copy of the latest *Pharmaceutical Recipe Book*.

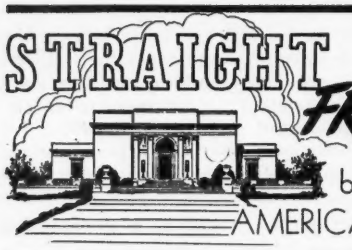
The work you are doing for the pharmacists in the government services is highly appreciated. We know that with your able direction the utmost in opportunities and benefits will be made available.

Washington, D. C. MAJ. KENNETH B. JOHNSON

Sirs:

I received the missing issues of the *Practical Pharmacy Edition* and *Scientific Edition* this past week. In going through these I found such a wealth of information that I am particularly grateful for having received every copy.

Brooklyn, N. Y. IRVING SCHERTZER



STRAIGHT FROM HEADQUARTERS

by ROBERT P. FISCHELIS, Secretary
AMERICAN PHARMACEUTICAL ASSOCIATION

GEOGRAPHY DOES NOT CHANGE PRINCIPLES

MUCH has been said and written about the difficulty men and women in one section of the United States have in understanding what goes on in other sections. Politicians speak of getting closer to what goes on at the grass roots and of being able to interpret properly the desires and thoughts of constituents in far-away places. Of course there is much to be said for the advantages of personal contact with people whom one represents, but the fundamental problems of pharmacy, for example, are not much different in San Francisco than they are in New York.

This fact is brought home to anyone who travels from one end of the United States to the other and contacts successive groups of practitioners of pharmacy in its various phases. It is further emphasized at conventions where men have a chance to meet and discuss problems of mutual interest.

What stands out as a result of these contacts is that patterns of procedure develop in various states for handling the problems of pharmacy which may differ greatly as a result of the difference in time and thought given to methods of procedure by those who are expected to set the pace and create the patterns. Take the matter of regulating the sale of drugs and medicines, for example. A few days ago we received a memorandum stating that iodine tincture, camphorated oil and aspirin had been added to the list of "simple household remedies and drugs" which may be sold without the supervision of a pharmacist in the state of Nevada. In New York or New Jersey the sale of such drug products without professional supervision constitutes a violation of the pharmacy act.

How will it be possible to maintain the status of professional supervision over the production and distribution of drugs and medicines throughout the United States if boards of pharmacy in the various states will not adhere to a uniform plan of classification of drugs as poisonous, dangerous and restricted?

It is argued that in states where there are large rural districts, with pharmacies few and far between, provisions must be made for availability of emergency remedies. Such emergency provisions need not take on a lowering of standards for the distribution of drugs. Emergencies usually involve calling a physician, and the doctor's emergency bag will take care of most such cases.

Buying drugs such as iodine, camphorated oil and aspirin ahead in preparation for emergencies can be taken care of in the same manner as the purchase of food and clothing. The farmer in the rural district goes to town to purchase certain articles of food, clothing and equipment. He can make his emergency drug purchases at the same time and keep them on hand to be replenished from time to time.

Investigation will almost invariably reveal that those who express the greatest concern about possible emergencies in rural sections are the wagon peddlers or general merchants who wish to usurp the prerogatives of licensed pharmacists by way of legal loopholes.

Of course, pharmacists are somewhat to blame for opening up loopholes in carefully planned state programs for controlling all professional services in the field of medical care. If it can be shown that unlicensed personnel is being permitted to dispense drugs in pharmacies without the immediate personal supervision of a pharmacist, the argument that such service is given routinely in a licensed pharmacy falls flat. Nevertheless the principle of limiting the distribution of drugs to professional supervision under any and all circumstances is sound and should be insisted upon by all law enforcement officials and by all segments of the profession of pharmacy and the drug industry because it is in the public interest.

WORK ON A. PH. A. RESOLUTIONS FROM 1947 CONVENTION

MUCH constructive planning was woven into the resolutions adopted by the AMERICAN PHARMACEUTICAL ASSOCIATION at the Milwaukee convention last August.

Among the tasks which have been set for the ASSOCIATION in the coming year are the following:

1. To provide active assistance to both the U. S. Army and the U. S. Navy in building their respective Medical Service Corps, with special reference to the Pharmacy, Supply and Administration Sections.

Both Army and Navy are now engaged in drawing up regulations for activating these new corps. Visits to Army and Navy Hospitals by pharmacist consultants are under way and mutually helpful information is being developed. Close liaison is being maintained between the A.PH.A. office and the offices of the Surgeons General.

The cooperation of colleges of pharmacy will be required to make available certain types of instruction for the commissioned pharmacy officers upon whom will depend the quality of Army and Navy pharmaceutical service.

2. To present to the next convention in San Francisco a program for future action based upon the findings of the National Pharmaceutical Survey.

This seems like a large order since the findings of the Survey will probably not become known officially until some time in April of 1948. However, the task is not as large as it may appear, because it is very unlikely that the Survey will bring to light any facts which are not quite well known to those who have made a careful study of pharmaceutical affairs and trends. What the Survey is expected to accomplish can be summarized in a few words.

It is expected to emphasize, with factual data to support its findings, the relation of the practice of pharmacy to the other health professions, to the drug industry and to the health and welfare of the people. It is expected to point out to what extent the educational and licensure program in pharmacy is meeting the requirements for pharmacists who can adequately perform the functions which belong to pharmacy. It is expected to point the way toward better service through better education and more adequate law enforcement.

In meeting these objectives the Survey will doubtless point to numerous shortcomings in the present structure of American pharmacy, and it is to remedy these that the AMERICAN PHARMACEUTICAL ASSOCIATION has called upon its Council to prepare a program for action.

3. To develop a continuing program in public health education calculated to take the fullest advantage of the pharmacy as an educational center on public health matters.

This program is being worked out in cooperation with the U. S. Public Health Service which requested the A.PH.A. to participate in its long-range public health program. This will be integrated with the rededication of National Pharmacy Week to the fight against cancer and will take in such programs as that of the American Heart Association in its endeavor to focus public attention on the possibilities for reducing premature deaths from heart disease. The program of the American Social Hygiene Association for the control of venereal diseases and other health programs involving the control of tuberculosis, infantile paralysis and the diseases of old age will all receive attention.

4. To continue the study of the administrative set-up of the Association in the light of the growing influence and importance of the Association's activities in many directions.

A Committee of Six representing the Council, the House of Delegates and the ASSOCIATION at large has been studying this problem for more than a year and is arranging a series of meetings to give further consideration to all phases of this problem.

5. To continue holding district meetings of the Association in sections of the United States where there has been no national convention and to bring to the members of state pharmaceutical associations the developments in professional pharmacy by arranging for an A. PH. A. program as a part of the regular state association convention. A limited number of such programs will be supplied in the coming year.

6. To study the effect of organization of employee pharmacists as a part of the labor union movement upon the recruitment for the profession and the quality of professional services rendered. This study is being approached with a full realization of its importance to the future of the profession.

These are the more important projects on which the House of Delegates and the General Sessions expressed themselves. They will be given preferred attention in the general program of activities.

Propyl Thiouracil

PROPYL thiouracil has now become generally available to treat hyperthyroidism. It may be expected to replace thiouracil rapidly due to the much lower incidence of untoward reactions from the propyl derivative. The antithyroid drugs do not represent a large prescription volume but the introduction of thiouracil and its derivative has a special significance to both pharmacy and medicine: (1) These drugs represent the first satisfactory and highly effective medication for hyperthyroidism. (2) They are the first prescription drugs valuable enough for general use which also hold sufficient potential toxicity to require, under law, a warning on all such prescriptions dispensed.

Prior to the introduction of thiouracil in 1946, hyperthyroidism had been a medical problem of long standing. In a discouraging percentage of cases the administration of iodine would not return the basal metabolic rate to normal or completely free the patient from clinical toxicity. Surgical removal of part of the thyroid gland was the standard therapy for advanced cases but remains a serious operation.

Hyperthyroidism or thyrotoxicosis (Graves' disease) results from over function of the thyroid gland. The excessive amount of thyroid hormone in the body is manifested by increased metabolic rate, various nervous effects, loss of weight, sometimes an increased pulse rate and other symptoms.

Research has been aimed at creating compounds that would suppress thyroid activity by inhibiting the formation of thyroid hormone and decreasing basal oxygen consumption in the body. Following early experiments with thiourea and other compounds, thiouracil evolved as the first antithyroid drug of this type to come into general use. The promise of highly effective therapy represented by thiouracil, and the challenge of its alarming untoward reactions, stimulated intensive investigation of derivatives.

It soon became evident that appropriate substituents on the thiouracil molecule would produce greatly increased activity. Anderson and his co-workers at the Stamford Research Laboratories of the American Cyanamid Co. synthesized many alkyl substituted thiouracils from β-oxo esters and thiourea.[1] These were tested pharmacologically in a collaborative project with Astwood and his associates at Harvard Medical School.

Reporting on the antithyroid activity of some 300 compounds, Astwood and VanderLaan concluded[2] that 6-ethyl-thiouracil and 6-*n*-propyl thiouracil are about ten times more active than thiouracil in animals. This was confirmed by British workers.[3] Astwood reported that propyl thiouracil seemed to have a more lasting effect than thiouracil and that it had a greater activity-toxicity ratio. The data showed that propyl thiouracil was more toxic than thiouracil on a weight basis. But it was less toxic in acute and chronic experiments when used in quantities of equivalent antithyroid effect.

Like thiouracil, propyl thiouracil is not considered a fundamental cure for hyperthyroidism. It is said to inhibit the production of thyroglobulin, in this way breaking the cycle of disturbed hypothalamic-pituitary-thyroid relationships.

Broadening Concept of Therapy

Propyl thiouracil acts effectively against all types of hyperthyroidism, whether these are represented by diffuse or by nodular goiter. It has not been found to be of any value in simple goiter. Until recently thiouracil therapy has been referred to as a preoperative treatment or a treatment where operation is contraindicated. With the accumulation of favorable reports and the introduction of propyl thiouracil, some clinicians are considering such therapy as other than a temporary or stopgap measure.[3] Some further

increase in prescription use of the drug for home administration may also be indicated by the trend away from hospitalization, except for severe cases,[4, 5, 6] due to the reduced danger of serious untoward reactions and to accumulated experience in the management of patients.

Dosage

It is difficult to determine the minimum effective dosage of propyl thiouracil. The opinion has been expressed that too little attention was given to this problem in the case of thiouracil.[2] Clinical trials indicate that there are considerable individual differences in dosage requirement and a wide variation in the rate of response. Consequently a more cautious dosage schedule in some early trials of propyl thiouracil may have brought about a somewhat slower remission of the hyperthyroid state than can be normally expected.[2, 7] Reveno agrees with Astwood's earlier estimate that in man propyl thiouracil is approximately five times as effective on a weight basis as thiouracil. Astwood used an initial dose of 75 mg. per day, reducing this amount by one-third or two-thirds for maintenance.[2] In further studies[4] he increased the initial dosage to 100 to 150 mg. daily (50 mg. every eight hours for severe cases and 50 mg. every twelve hours for moderate cases).

Improvement may appear in a few days but many patients require months for complete disappearance of clinical signs. When hyperthyroidism has been brought under control the patient is placed on a maintenance dose, which Astwood indicates may begin at the level of 75 mg. a day in divided doses. This may be reduced later to 50 mg., and then continued for at least six months on the minimal dose that the physician finds consistent with normal thyroid function.[4] Most physicians establish adequate maintenance dosages by determining the basal metabolic rate.

At some time after complete withdrawal of the drug a certain percentage of patients relapse. Lahey's findings[10] point toward permanent remission in mild cases and toward expected recurrence in instances where the hyperthyroid state was more advanced. Astwood[4] believes that the majority of patients will remain well for an indefinite period if they have remained in good health on minimal dosage for at least six months. Other than the usual possibility of an untoward reaction, there appears to be no reason why treatment could not be resumed whenever necessary and no indication that harm results from long-continued therapy.[4,5]

The arbitrary period of six months or so of normal health, on minimal dosage, has been recommended as the preferred criterion of the proper duration of treatment, rather than an estimate based upon the total period of treatment.

Bierwaltes and his associates[8] support the view that an initial dosage of 150 mg. daily is adequate to bring hyperthyroidism under control in most patients. On the basis of a statistical analysis of clinical data, they find no advantage in increased propyl thiouracil dosage above this level. In their study the basal metabolic rate of 42 patients receiving 0.15 Gm. propyl thiouracil daily was charted against that of 98 patients who had received 0.6 Gm. thiouracil daily. The rate of descent of the basal metabolic rate was almost identical in the two groups.

If the patient takes excessive doses of propyl thiouracil signs of hypothyroidism appear, followed by myxedema, which is marked by such symptoms as dropsy-like swelling, slowing of the pulse rate and sluggishness. Reducing the dose or temporarily withdrawing the drug ordinarily permits prompt recovery.

Within the normal dosage range, untoward reactions from propyl thiouracil have been infrequent. This represents a marked advance in therapy since about 13% of hyperthyroid patients on thiouracil show some adverse reaction.[9] The most serious, and sometimes fatal, complication from administering compounds of this type is granulocytopenia. With thiouracil this occurred in about 2.5% of treated patients, which is the principal justification for an ever-present warning on the prescription label.

Granulocytopenia is marked by a white cell count less than 4000 or 4500, and marked reduction in granulocytes, associated with sudden onset of acute symptoms such as fever, sore throat, prostration and malaise.

Untoward Reactions

Propyl thiouracil has the potentiality to induce this and other types of toxic reactions noted with thiouracil, although only isolated instances of white cell depression appear to have occurred so far.

Bierwaltes[8] states that "since propyl thiouracil lacks toxicity mainly by virtue of its decreased dosage, the occurrence of the more severe forms of toxic reaction—such as agranulocytosis and drug fever—might be logically expected as the amount of drug administered is increased."

McCullagh and his associates[6] reported one case of white cell depression as the only untoward reaction in a series of 110 patients; Lahey[10] observed five cases of white cell depression in-

cluding one case of agranulocytosis among 300 patients; and Bartles has been quoted[8] as having encountered three cases of agranulocytosis presumably due to propyl thiouracil. Because of the possibility of this serious complication, however remote, most clinicians and the manufacturers of the drug recommend regular observation of patients with frequent laboratory checks on the white blood cell count, including differential counts.

The treatment of agranulocytosis is withdrawal of the drug, administration of massive doses of penicillin, 500,000 units per day, and transfusions of fresh whole blood.

Apparently one of the most frequent untoward reactions so far observed with propyl thiouracil is dermatitis. Bierwaltes[8] observed one instance of this among 42 patients treated; and the only other possible untoward reaction reported by patients was a drowsiness.

McGavack and his co-workers[11] noted one reaction, among 75 patients, in the form of pruritis accompanied by fever. This patient was known to be sensitive to thiouracil also. A rash was noted in one patient out of a series of 16 reported on by Wilson and Goodwin.[12]

In a report on 54 patients treated Reveno[7] noted one untoward reaction, a case of drug fever requiring withdrawal of the drug. Astwood[5] reported four instances of itching skin among 100 patients, two with frank urticaria. In no instance was it necessary to abandon therapy.

It is significant to note that several investigators employing propyl thiouracil report successful treatment of patients known to be sensitive to thiouracil.[2, 5, 7] Recently, however, a case was reported where mild leukopenia, induced by six months of thiouracil therapy, developed into severe leukopenia four months after treatment was shifted to propyl thiouracil.[15]

Clinical Experience

Clinicians apparently agree that the management of patients on propyl thiouracil and the therapeutic response are similar to that with thiouracil. Response to either drug is apt to be delayed when the patient previously has been on iodine therapy. When propyl thiouracil is used, clinicians rarely continue other specific treatment. Astwood[5] states that established iodine therapy may be discontinued abruptly in most patients, although in severe cases it should be withdrawn gradually during the first seven to ten days on propyl thiouracil.

From clinical experience at the Pratt Diagnostic Hospital it was concluded that propyl thiouracil has made "treatment of thyrotoxicosis a simple and safe procedure that can be carried out by any practitioner of medicine. Only the most severe cases require hospital care. . . . It is now apparent that antithyroid therapy is not just a temporary measure or one to be used before surgery, but a definite treatment in itself, one which gives rise to sustained remissions in a large proportion of cases. Surgical procedures are considered to be unnecessary except in rare instances for appearance sake."[4]

It has not been established, however, that remissions of the hyperthyroid state, induced by propyl thiouracil, are permanent. In view of this, considerable difference of opinion has developed concerning the proper scope of therapy. Lahey[10] and his supporters feel that there is still no convincing evidence that such treatment ordinarily should be considered an acceptable substitute for surgery.

Lahey points out that use of the thiouracils as a preoperative treatment has made thyroidectomy a safer procedure. In his clinic iodine is given routinely in combination with propyl thiouracil to produce involution that devascularizes the gland and makes conditions more ideal for surgery. Propyl thiouracil may be discontinued a week before operation as a safeguard against the possibility of white cell depression at the time of surgery.

It is evident that a longer period of clinical trial and observation must elapse before there will be a clear indication of the extent to which propyl thiouracil therapy should be considered a replacement for surgery.

A prominent feature of thyrotoxicosis that may be slow to improve under therapy is exophthalmos ("popping out" of the eyes). The cause of exophthalmos is unknown and there is no specific treatment. The best treatment appears to be complete control of the associated hyperthyroidism.

The generally reliable response of the hyperthyroid state and the apparent infrequency of significant untoward reactions from proper use of propyl thiouracil led to such confidence by one of the leading investigators that his patients "were not warned of any dangers associated with drug therapy [and] were usually seen every few weeks until the hyperthyroidism was controlled and then at two- to three-month intervals thereafter."[5]

Adoption of any such optimistic view among physicians would appear to be out of harmony with the responsibility placed on the pharmacist by the Food and Drug Administration to warn patients about potential ill effects from the

drug. The required warning appears on commercial packages of propyl thiouracil and must be transferred to prescriptions, with or without the consent of the prescribing physician.

Warning Notice Requirement

This new departure in prescription labeling was introduced by the type of warning required for thiouracil, and is being continued in modified form for propyl thiouracil.

The original ruling on the thiouracil warning was considered objectionable by the AMERICAN PHARMACEUTICAL ASSOCIATION[13] not only because the pharmacist was asked to place on a prescription instructions not requested by the physician, but because the proposed warning identified the drug prescribed, named symptoms to be watched for, and seemed more alarming to the patient than necessary.

The F.D.A. maintained, however, that legal interpretation of the Federal Food, Drug and Cosmetic Act indicated that the potential dangers from thiouracil made it "an outstanding example of those relatively few drugs where a warning on the prescription labeling is essential to the 'protection of users.' "

Although recognizing that here was a drug only available because its unusual value outweighed its dangers, representatives of the AMERICAN PHARMACEUTICAL ASSOCIATION remained convinced that the particular warning required was unsatisfactory. This view received support by the Council on Pharmacy and Chemistry of the American Medical Association and by a conference of medical and pharmaceutical representatives called by the Council.

Eventually a revised warning was proposed by the Food and Drug Administration for propyl thiouracil, and thiouracil, which reads as follows:

"*Warning:* This drug may cause unfavorable reactions in some individuals. Your physician has explained or will explain to you the symptoms which must be watched for and precautions which must be taken to guard against ill effects. Do not take in larger doses, or more frequently, or for a longer time than specifically directed by the physician."

THE AMERICAN PHARMACEUTICAL ASSOCIATION has expressed its "approval of the general principles underlying the revised form of warning notice."[14]

In dispensing propyl thiouracil (or thiouracil) prescriptions the pharmacist is obligated to comply with the warning requirement. This might be accomplished by (1) using printed stickers, (2) leaving the manufacturer's warning affixed to the bottle if the original container is dispensed, or (3) affixing a typed warning somewhere on the dispensing container.

It will be noted that the warning implies positive action on the part of the physician to inform patients of possible reactions and precautions that should be taken. As a point of professional courtesy it would be well to inform the prescriber that the warning is being placed on his propyl thiouracil prescriptions. If the physician expresses doubt concerning the wisdom of this procedure, the pharmacist should explain the need for it under the law and perhaps recall to the physician's attention that caution seems indicated by the close relationship of propyl thiouracil to thiouracil. The newer drug is presumed to have the potentialities for the same type of toxic reactions as its predecessor, at least in certain patients under certain conditions of use. This fact, and the nature of the indications for which the drug is used, also show the need for checking with the physician before refilling prescriptions.

Summary

1. Many substituted thiouracils have been prepared in an effort to obtain a more effective or safer antithyroid drug. Of these, 6-*n*-propyl-2-thiouracil has been evaluated clinically as the present drug of choice.

2. Propyl thiouracil is prescribed as a preoperative treatment or where thyroidectomy is contraindicated. It is also coming into use as a preferred substitute for surgery, but its proper position in this field has not been established.

3. On the basis of clinical results to date, pharmacists may expect prescriptions to specify an initial dosage up to 150 mg. per day in divided doses, with significantly higher doses being reserved for severe or recalcitrant cases. After the hyperthyroid state has been brought under control, the prescribed maintenance dose may vary widely among individuals but will frequently be in the neighborhood of 50 to 75 mg. daily.

4. Propyl thiouracil marks a distinct advance over thiouracil because the incidence of untoward reactions is much lower, according to present evidence. It is actually more toxic than thiouracil by weight, but has about five times the therapeutic potency of thiouracil in man.

5. Propyl thiouracil requires a warning notice on all prescriptions dispensed, since it is closely

(*Continued, page 620*)

Cardiac Therapy

by HARRY GOLD, M.D.*

I HAVE planned to present an account of pharmacologic studies which have a more or less direct bearing on problems of cardiac therapy. I shall confine my remarks, for the most part, to explorations in this field which have been made in recent years by a group of collaborators in our laboratory and clinics.[1] These relate chiefly to investigations made directly on human subjects.

The term "clinical study" doesn't rate very high in scientific circles. The belief prevails that the search for facts on drug action in man directly is of necessity inexact, subject to the impressions and prejudices of the observer and not amenable to the strict control of the animal experiment. There are, to be sure, many problems in pharmacology which are inaccessible to study directly on the human subject, but there is a vast area of pharmacologic investigation which may be developed with the human subject and which, if the experiments are suitably designed, may be counted on to yield important facts in a manner which complies with the strictest demands of scientific evidence.

Action of Digitalis in Failure.—How digitalis acts to relieve heart failure has long been a matter of controversy. No doubt exists that the failing heart is able to perform more effectively under the influence of digitalis. However, we were very long in obtaining an answer to the question whether digitalis glycosides act directly on heart muscle to increase the systolic force or whether the action is entirely indirect.

A few years ago an answer to that question was supplied by means of simple preparation of the mammalian heart muscle.[2] The papillary muscle of the right ventricle of the cat, a muscle about 10 mm. long and weighing about 20 mg., was set up on an isometric lever, driven at a fixed rate, and its tension recorded photographically. The muscle soon began to fail, and when its force had fallen to a very low level a digitalis glycoside was administered in a concentration prevailing after therapeutic doses in man, as low as 1 part in 75 million parts of fluid. Within several minutes the force began to rise and reach high levels, at which it remained for many hours.

No other chemical material is known which produces such definite and sustained increase in the systolic force of the mammalian heart muscle. While the systolic force rose, the "tone" of the muscle remained unchanged. An increase in the systolic force measured by its tension, as a result of a direct action on the heart muscle, may therefore be taken as the primary mechanism by which digitalis relieves heart failure. Most of the other significant changes in the heart and circulation which occur in patients with heart failure after digitalis follow as secondary adaptations.[3]

Vagal and Extravagal Action of Digitalis.—Slowing of the ventricular rate is one of the outstanding results of digitalis action in auricular fibrillation. Two mechanisms may be seen to be at work.[4] In some instances blocking the vagus by 2 mg. of atropine sulfate intravenously abolishes the slowing, while in others the atropine has little influence on the slowing.

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In a further study of the matter we found that in one and the same person the slowing may be vagal at one time and extravagal at another and further that the deciding factor is the dose of digitalis. As the dose is increased the control of the ventricular rate tends to pass from the vagal to the extravagal mechanism. It is important to note that in the operation of this adaptive mechanism the resting rate may remain unchanged.

In another investigation[5] we observed that physical exercise to the limit of the patient's endurance has the same effect on rate as blocking the vagus with atropine. When slowing is by the vagal mechanism (abolished by atropine) exercise may accelerate the rate to 180 a minute, but when the slowing is by the extravagal mechanism (not abolished by atropine) exercise rarely accelerates the rate above about 100 a minute.

This is a matter of some importance in the maintenance of patients with auricular fibrillation. In the treatment of these patients it is not uncommon to find digitalis reducing the rate from 140 to 70 when the patient is at rest. When he is up and about, however, he complains of palpitation and breathlessness. Free physical activity raises the rate to uncomfortable peaks when the mechanism of control is vagal. If larger doses of digitalis are given, the rate control passes to the extravagal mechanism, which prevents the exaggerated acceleration with exercise, even though the resting rate may not be materially lowered. These mechanisms are illustrated diagrammatically in Fig. 1 on the following page.

U. S. P. Assay of Digitalis.—The potency of digitalis preparations is known to vary. The latest revision of the U. S. Pharmacopœia adopted the cat method of assay as a means of securing uniformity. In this method the unknown preparation and the Standard Reference Digitalis are injected intravenously into cats and the ratio of their lethal doses is determined. The unknown is so adjusted that 0.1 Gm. produces the effect of 0.1 Gm. or 1. U. S. P. unit of the Standard. This is by intravenous injection in cats. But digitalis preparations differ in their absorbability, and they are usually given by mouth in man. A material that is potent by vein may be weak by mouth if it is poorly absorbed.

Human Assay of Digitalis.—To overcome this difficulty we developed a method for the assay of digitalis preparations by oral administration in man,[6, 7] following basic principles of bioassay.

How different are the answers by the two methods of assay? We have secured some idea about that from a series of preparations which were tested by the two methods. (The results are shown in Table 1 on page 598.) Imagine each of these preparations put up in a tablet of 1. U. S. P. unit as determined by the official intravenous cat method. For different specimens of digitalis labeled 1 U. S. P. unit one tablet may produce three times as much effect as another, and in the case of purified glycosides one tablet may produce about ten times as much effect as another.

This matter is quite serious if it is not clearly understood, for 10 U. S. P. units of lanatoside C (Cedilanid) would be insufficient to digitalize a patient, whereas 10 U. S. P. units of digitoxin might prove fatal. The human method of assay seems to be the only present remedy to the problem of securing uniformity of digitalis preparations for oral administration in man.

Absorption of Digitalis Glycosides.—We may now turn to the subject of the absorption of digitalis materials from the gastrointestinal tract. We approached the study of this matter by comparing the size of the oral and intravenous doses necessary to produce the same effect in patients with auricular fibrillation. This ratio of oral to intravenous dose is a practical index of absorption for the vast majority of digitalis materials. The patient is put to bed, the ventricular rate is

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DO YOU KNOW—

- ***Why relatively large doses of digitalis result in minimum discomfort from exaggerated heart rate during physical activity?***
- ***The advantage of the human assay method for digitalis, and why U. S. P. unitage is often not a reliable guide for oral dosages?***
- ***How and why the physician can safely achieve single-dose digitalization?***
- ***What is meant by the "ceiling effect" of cinchona alkaloids?***
- ***The limitations and true significance of an "average dose"?***
- ***How the physician could use mercurial diuretics to better advantage?***

—In the accompanying paper an authority on cardiac therapy gives his answer to these questions based on investigations that shed new light on problems that have surrounded treatment of the failing heart.

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counted several times daily during a control period, and, when the rate has stabilized, a large dose is given at one time by mouth or by vein as the case may be, and similar counts of the ventricular rate are made at frequent intervals during the day until the full effects have developed.

FIG. 1.—Schematic representation of the mechanism by which digitalis slows the ventricular rate in heart failure with auricular fibrillation.

By means of this method it was found that digitoxin is practically completely absorbed[8] (fig. 2), since a dose produces the same effect whether given by mouth or by vein. About 20% of a dose of digitalis is absorbed, and only about 10% of a dose of lanatoside C (fig. 3). Complete absorption from the gastrointestinal tract is a rare experience in pharmacology. There are very few drugs for which the oral and intravenous doses are the same.

Single Average Full Dose Method of Digitalization.—The human assay of digitoxin by the T-wave shows that 1 mg. produces the same effect in man by oral administration as 1 Gm. of the Standard Digitalis Powder. The same relationship was found to apply to the effects in auricular fibrillation[8] (fig. 4). The fact that digitoxin is so potent and so well absorbed suggested the possibility of employing it in a single dose method of digitalization to replace the multiple dose methods employing digitalis leaf or the tincture.[9]

Our results indicate that the most favorable routine technique for digitalizing patients is to administer 1.2 mg. of digitoxin at one time. This produces a high degree of digitalization in a period of about six to ten hours in the place of the twenty-four to forty-eight hour period required for the divided dose methods in which digitalis is used. One cannot use the digitalis leaf or the tincture by this method, because the equivalent amount of digitalis, namely 1.2 Gm., will cause nausea or vomiting by local action in about 10 to 20% of the cases. The therapeutic effects are maintained in the majority of cases by a single daily dose of a tablet of 0.2 mg. The use of digitoxin in this way has greatly simplified the problem of digitalization.

Variations in Human Susceptibility to Digitalis.—Some difficulty has been encountered in gaining general acceptance of the idea that it is proper to use an average full digitalizing dose of digitoxin at one time in a routine manner. The argument is that patients vary too much, that the most tolerant ones will escape full digitalization and the most susceptible ones will be poisoned. It is indeed a fact that some patients need closer to 2 mg. to digitalize them fully. From our experience with more than 1000 single dose digitalizations with 1.2 mg. a negligible number, about 2 out of 100, show nausea or vomiting. The safety of this method is therefore beyond question.

In this connection I may call attention to a fact pointed out by Clark[10] and others that digitalis action in animals is very uniform as drugs go. We recently prepared a distribution curve of digitalis action after oral administration in 86 patients (833 doses) based on the threshold doses causing a T-wave change in the electrocardiogram.[11] The curve is very similar to that observed in the cat. Variation of patients' sensitivity from the approximate mean is not great. A dose ±25% of the mean includes about 70% of the cases. Such variations in dosage are hardly detectable in clinical digitalization. A dose ±50% of the mean, which would hardly be expected to cause either serious underdigitalization or overdigitalization, includes more than 90% of the cases. There

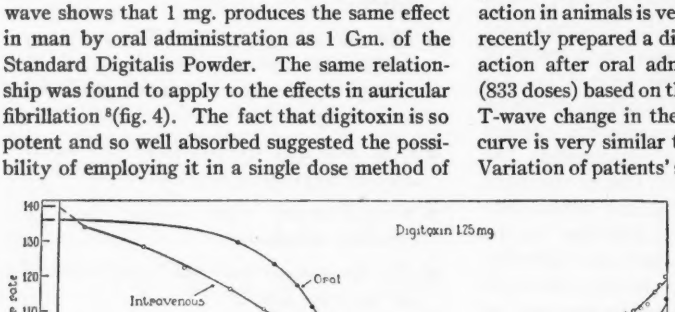

FIG. 2.—Comparison of digitoxin by oral administration and intravenous injection in patients with heart failure and auricular fibrillation. Time is charted in hours after the dose. Curves represent the average results with 9 (oral) and 14 (intravenous) patients.

is therefore a sound pharmacologic basis for the validity of the single average full dose method of digitalization.

What was needed was a preparation of digitalis which could be given in that way without irritating the stomach. As I have already indicated, digitoxin meets that need because of two characteristics. It is so potent and so well absorbed that the approximate mean oral digitalizing dose involves only 1.2 mg. of glycoside, an amount too small to cause local gastrointestinal irritation, also an amount smaller than that required for any other glycoside in common use at the present time.

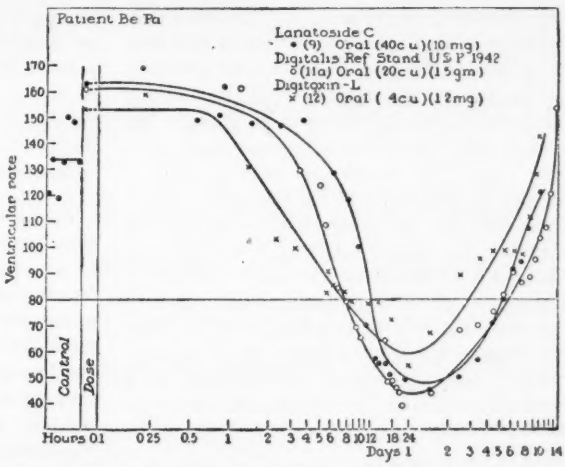
Patient Be Pa
Lanatoside C
• (9) Oral (40c u)(10 mg)
Digitalis Ref Stand U S P 1942
δ (11a) Oral (20c u)(1 5gm)
Digitoxin-L
× (12) Oral (4cu)(1 2mg)
Ventricular rate
Control
Dose
Hours 0 1 0 25 0 5 1 2 3 4 5 6 8 10 12 18 24
Days 1 2 3 4 5 6 8 10 14

FIG. 3.—Absorption of several digitalis materials in patient with heart failure and auricular fibrillation. Note that substantially similar effects result from 4 cat units of digitoxin, 20 of digitalis leaf and 40 of lanatoside C, owing to differences in absorption.

Cumulation.—The term cumulation is widely applied to the action of the digitalis bodies. It is usually taken to refer to the fact that, if a particular dose which in itself causes little or no effect is given repeatedly, an effect will soon appear and increase in intensity as the dose is continued. There is considerable controversy concerning the precise nature of the phenomenon. We have made some observations which suggest that it represents gradual accumulation of the drug resulting from the fact that elimination falls behind. The behavior of the phenomenon resembles closely the cumulation of other drugs which are slowly excreted, such, for example, as the bromides.

If one gives a dose of sodium bromide daily, say about 1 Gm., the bromide concentration of the blood begins to rise, going up to 5, 10, 20, 30, 40 mg. per hundred cubic centimeters. As the dose is continued, however, the cumulation soon comes to an end and the blood concentration continues at that level no matter how long the daily dose of bromide is continued. Cumulation is therefore a self-limiting process when a fixed daily dose is administered.

The same is true of digitalis, although we do not determine it in terms of milligrams of drug but in terms of a pharmacologic effect.[12] This phenomenon was illustrated by a group of patients with auricular fibrillation. They received a single daily dose of 0.2 mg. of digitoxin. As the dose was repeated, the ventricular rate began to decline. It continued to fall for a period of about two to three weeks, after which it leveled off even though the dose was continued for eight or ten weeks longer. It is clear, therefore, that a fixed daily dose of digitalis produces cumulative effects which are self-limiting in a manner similar to that of the bromides. When the dose was discontinued, the effects began to wear off and disappeared completely in about three weeks, resembling in this respect the effects of one large dose.

The time it takes to reach the level varies with different drugs. In the case of quinidine, a fixed daily dose shows increasing effects during

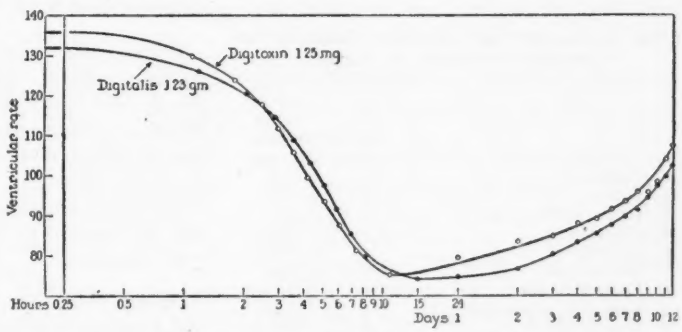

FIG. 4.—Comparison of oral digitoxin and digitalis in 9 patients with heart failure and auricular fibrillation. The drug was given in one dose. Time is charted in hours after the dose. Note the similarity in speed of absorption and duration of action of digitalis and digitoxin.

only the first three or four days. The effect then levels off, so that the continued use of that dose for months fails to produce any greater effects.

The practical importance of this phenomenon is clear enough. In the use of digitalis the patient receiving a fixed daily dose needs to be observed for from two to three weeks for signs of increasing intensity of action that may lead to poisoning. On the other hand, in the case of quinidine it is only a matter of a few days. If the fixed daily dose does not produce the desired therapeutic effects or poisoning within three or four days it is very unlikely that it will do either if continued for months unless the dose is increased, since the highest concentration on a fixed daily dose is reached within a few days in the case of this drug.

Comparison of Drugs.—I have described the method of assay of digitalis. In principle it means simply determining by how much one preparation is stronger than another, the standard preparation. Materials other than digitalis present the same problems. Let us see what has happened in the case of cinchona alkaloids.

Frey[13] in some clinical observations in 1918 showed that quinidine is more effective than quinine in abolishing auricular fibrillation. Lewis and his collaborators[14] in 1921 made experiments in which the difference received a quantitative expression. Their conclusion that quinidine is five to ten times as effective as quinine in slowing the circus movement in the auricle has been widely quoted in the textbooks in the last twenty-five years. The implication is that all one needs to do is to give five to ten times as much in order to obtain the same results. They found that as the dose of quinidine was increased the effect increased, but at about 0.8 Gm. a ceiling was reached. If two compounds are compared at the dosage level of 0.8 Gm. or larger, and the effects are the same, one may still be many times as potent as the other, but the difference escapes detection because, at the ceiling effect, differences cannot be revealed. And it is at this very level of dosage, namely 0.8 Gm., that Lewis and his collaborators compared these drugs.

TABLE 1—POTENCY OF DIGITALIS MATERIALS BY DIFFERENT METHODS OF ASSAY

	Preparation	U. S. P. Unit (Cat Method)	U. S. P. Units (Human Method)
1.	Digitoxin	1	5.55
2.	Gitalin	1	1.81
3.	Indian urginin	1	0.51
4.	Lanatoside C	1	0.50
5.	Digitalis leaf	1	0.56
6.	Digitalis leaf	1	0.59
7.	Tincture digitalis	1	0.76
8.	U. S. P. XI reference digitalis	1	0.80
9.	Digitalis tablets	1	0.87
10.	H. A. No. 9 leaf	1	0.87
11.	Digitalis leaf	1	0.95
12.	Digitalis tablets	1	0.97
13.	Digitalis leaf	1	1.46

Dosage Response Curve.—We have repeated these studies[15] with dosage response curves. Out of the preliminary experiments a somewhat different story is beginning to emerge. Indeed, the results confirm the observation that quinidine is more effective than quinine, gram for gram. As the dose is increased the effect in the case of each drug increases, and in each case a ceiling effect is reached. But it was also noted that the ceiling is about twice as high in the case of quinidine as for quinine. Therefore, in the range of a low-grade effect, the two drugs are interchangeable. In case the therapeutic effect can be secured by an action equal to circus slowing in degrees up to 20%, either drug will produce it if one uses two to three times as much quinine, but if stronger actions are necessary in the range shown by circus slowing up to 40% the two drugs are no longer interchangeable. No matter how much quinine is given it cannot match the effect of quinidine in this range. It cannot exceed its own ceiling. The case of ephedrine and epinephrine on the blood pressure would yield a similar set of results.

I wish to call attention to the fact that the comparison of drugs is a pharmacologic game with a set of rules which must be observed. The results do not come out right if the rules are ignored. The dosage response curve, which is the only means of securing information regarding the sensitive range of the physiologic measuring device, is not commonly established in the usual comparisons of drugs on the human subject.

Dosage.—We might now turn to another matter concerning the use of cardiac drugs, namely, the principles of dosage. The case of digitalis, quinidine and the mercurial diuretics may be used to illustrate my points, although it goes without saying that basic principles of dosage which operate in the case of these might well be expected to find application to therapeutics in general.

Average Dose.—I have already discussed the use of digitalis in the form of an average digitalizing dose given at one time. The term average dose is freely used in the clinical literature, but

(*Continued, page 622*)

PRESCRIPTION

Accuracy and Tolerances

SECOND IN A SERIES ON STANDARDS FOR PHARMACEUTICAL COMPOUNDING; NEED SEEN FOR OFFICIAL CLARIFICATION OF "REASONABLE" TOLERANCES

by SAMUEL W. GOLDSTEIN*,†

THE person who graduates from an accredited pharmacy college is well trained. We expect him to have the background required for licensure and a professional career. If he then conducts himself in accordance with the Code of Ethics of the AMERICAN PHARMACEUTICAL ASSOCIATION,[1] the pharmacist deserves professional recognition.

He can practice professionally either in a so-called "professional pharmacy" or in a "drug-store." Most pharmacists in either type of establishment, we believe, conduct their professional practice competently. There are some who do not; and there are such practitioners in every profession.

Yet, pharmacy may well be concerned about some recent unfavorable publicity based on factual data purporting to show that pharmacists do inaccurate work when called upon to compound medicinal preparations. The few public health officials concerned are perfectly sincere in their criticisms but do not seem completely aware of all the problems confronting pharmacists.

Their data were obtained by studying analytical results of tested prescriptions and other extemporaneous preparations compounded by pharmacists in several states.[2–5] Classification of preparations as standard or substandard was based upon whether they met U. S. P. and N. F. tolerances in the case of official preparations, or whether they met a tolerance of ±10% in the case of unofficial preparations.

It will be universally conceded that compounding prescriptions or other extemporaneous preparations requires adequate professional and scientific knowledge, and that a "reasonable" degree of accuracy is essential. Two questions then arise: (1) Are there specific reasons why criticism of accuracy in compounding is coming from public health officials who are not pharmaceutically trained? (2) What is reasonable accuracy in compounding?

Pharmacists are not being criticized because they play a vital role in guarding public health by using their knowledge of posology and pharmacology. Let us not forget that it is after studying the prescription, with the dosage as the most important factor, that the preparation is compounded. (No figures are available to show how many times in the course of filling about 300,000,000 prescriptions a year pharmacists have called errors to the attention of prescribers.) We have pointed out, however, the possible relation of the pharmacist's knowledge of dosage range and inaccurate home-methods of administering prescription medication, to the factor of carelessness in compounding. Other factors that affect pharmaceutical accuracy—which must be considered in an evaluation of accuracy—have also been discussed in a preceding paper.[5]

The answer to the first of the two above questions is that *pharmaceutically trained* public health officials do not adhere strictly to the official or ±10% tolerances in classifying tested preparations. This can be illustrated by data obtained from the tested drug samples (manufacturer's samples included) shown in Table 1. This table covers a period during which the position of State Drug Commissioner was occupied by three pharmaceutically trained men. Apparently these three men interpreted analytical data, in terms of illegal samples, in a similar manner.

The first column shows the yearly percentage

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† The conclusions and recommendations appearing in this paper represent the personal opinions of the author.

TABLE 1—RELATIONSHIP OF TOLERANCE INTERPRETATION AND ILLEGAL SAMPLES

YEAR	SUBSTANDARD PREPARATIONS IN %; "REASONABLE" INTERPRETATION	SUBSTANDARD PREPARATIONS IN %; STRICT INTERPRETATION
1937	5	14
1938	4	7
1939	5	14
1940	9	14
1941	13	19
1942	14	20
1943	13	21
1944	13	21
1945	9	20
1946	9	18

of substandard preparations. It is based upon the pharmaceutically trained, pharmacy law enforcement officer's interpretation of the analytical data for more than one thousand samples each year.

The second column shows the percentage of substandard preparations for the same year and the same preparations based upon strict adherence to the set tolerances.

Results obtained from analyses of prescriptions filled by pharmacists are shown in Table 2.

By interpreting the analytical results strictly on the basis of a ±10% tolerance, 52% of the prescriptions tested are substandard; while more reasonable interpretation places 30% outside the legal limits.

TABLE 2—PRESCRIPTIONS. EFFECT OF TOLERANCE INTERPRETATION

YEAR	NUMBER OF PRESCRIPTIONS ANALYZED	NO. SUBSTANDARD, "REASONABLE" INTERPRETATION	NO. SUBSTANDARD, STRICT INTERPRETATION (±10%)
1940	10	1	1
1941	8	0	2
1942	28	14	20
1943	2	0	1
1944	4	2	2
1945	6	0	4
1946	7	3	6
1947*	6	1	1
Totals	71	21	37

* Through April only.

Table 3 is restricted to pharmaceutical preparations extemporaneously compounded by pharmacists and purchased in drugstores during 1945 and 1946.* It may be seen that the relationship between the "reasonable" and the strict interpretations is similar to that shown in Table 1.

TABLE 3—EXTEMPORANEOUS PREPARATIONS. EFFECT OF TOLERANCE INTERPRETATION

PREPARATION	YEAR	NO. OF SAMPLES ANALYZED	% SUBSTANDARD, "REASONABLE" INTERPRETATION	% SUBSTANDARD, STRICT INTERPRETATION
Acet. Ac. Sol. 10%	1945	57	19	47
Boric Ac. Sol. N. F.	1945	63	13	18
Chloroform Spirit	1945	14	0	50
	1946	40	22	26
Dil. Hydrochlor. Acid U. S. P.	1945	49	22	38
	1946	40	12	38
Lime Water U. S. P.	1945	82	4	12
	1946	71	3	4
Lugol's Sol. U. S. P.	1945	77	10	13
	1946	135	7	13
Neo-silvol Sol. 0.25%, 0.5%	1946	25	16	28
Phenacetin Capsules 5 gr.	1945	32	25	38
Phenol in Oil 2%	1944	37	54	54
Phenol Ointment 2%, 5%	1944	27	48	48
	1945	37	24	46
Pot. Iodide Sol. N. F.	1945	195	8	28
	1946	80	9	31
Pot. Permang. Sol. 2%, 3%, 3.5%	1945	133	8	17
	1946	105	11	24
Salicyl. Ac. Ointment 2%, 2.5%, 3%, 5%	1945	105	10	25
	1946	72	11	29
Silver Nitrate Sol. 1%, 2%	1945	186	9	18
	1946	192	9	22
Silver Proteinate Sol. 0.25%, 0.5%, 1%	1945	10	0	10
	1946	77	5	19

The data given in Tables 2 and 3 show that a "reasonable" interpretation of analytical data lowered the percentage of extemporaneous preparations and prescriptions classed as substandard to a marked extent.

We have seen how two different pictures can be drawn from the same data, depending upon how the analytical results are interpreted. Now we can go on to the second question: What is a "reasonable" accuracy? Here the viewpoint of the individual will enter into the definitive answer. Scientifically trained men, accustomed to

* Only those preparations of which ten or more samples were analyzed are given. In the case of phenol preparations, two groups of samples analyzed in 1944 are included.

the accuracy of the control laboratory, will say that the tolerances allowed in the official compendia are reasonable. It will be maintained that official tolerances should be met by the pharmacist in the drugstore as well as by the manufacturing pharmacist.

The scientifically trained pharmacist cannot help but see that the presently accepted tolerances are fair enough when applied to preparations manufactured under controlled conditions by reliable drug manufacturers, or to preparations manufactured in large quantities in the drugstore. (Lime water U. S. P. is one of the latter preparations and it shows the lowest percentage of substandard samples of all the tested extemporaneous preparations.) It also seems clear, in my opinion, that these same tolerances cannot be applied fairly to extemporaneous preparations compounded in small quantities from ingredients having different degrees of stability and manipulative flexibility.

It appears that the different percentages of unsatisfactory samples, representing data covering the same samples, reflect an effort to weigh the analytical results in an honest and logical manner in relation to such factors as the quantity of the preparation and inherent manipulative difficulties. The percentages representing a "reasonable" interpretation are naturally in the direction of liberalizing an official or ±10% tolerance in most cases.

Here then is given semi-official state recognition to the fact that in at least many instances the present tolerances are too stringent when applied to extemporaneous preparations. Why should this procedure be followed tacitly? It would be much better to have reasonable tolerances established and given general recognition through a careful, quantitative study of extemporaneous compounding. Then why not have such reasonable tolerances officially recognized by a statement in the U. S. P. or N. F.?

These steps should be taken so that the work of the pharmacist will be judged on a reasonable basis by all persons interested in pharmaceutical accuracy. There appears to be evidence that too many pharmacists frequently will not meet reasonable tolerances; there likewise appears to be evidence, however, that unreasonable tolerances are sometimes applied to prescription practice in evaluating accuracy. This reveals the need for a sound program to indicate where attention must be given to elevating further the level of prescription accuracy and where present criticisms may be justly tempered.

Summary

1. The professional status of pharmacy is recognized and upheld.

2. The basis for current criticism of pharmaceutical accuracy is discussed.

3. Data are given to show that some pharmaceutically trained drug control officials liberalize present official tolerances in classifying prescriptions and other extemporaneously compounded preparations as legal or illegal, depending on the particular difficulties apparently encountered in retail practice.

4. The necessity for a careful study to establish "reasonable" tolerances in extemporaneous pharmaceutical compounding, and for official recognition of such tolerances, is discussed.

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REMOVING PAINTED LABELS FROM TUBES

REMOVING from manufacturers' ointment tubes the painted labels, to be replaced by a prescription label bearing the physician's directions, represents a source of annoyance in the busy prescription laboratory. Mr. William P. O'Brien, New Orleans pharmacist, suggests a method for removing such labels as a simple, time-saving point of technique.

An eight-ounce, wide-mouth, screw-cap, powder jar containing one-third to one-half its volume of chloroform is used. A dispensing tube which bears a painted label is placed in the jar cap up, and the cover of the jar is then screwed on tightly.

The jar is set aside for a few minutes, or just long enough to prepare the prescription label. Then the jar is gently rotated to facilitate removal of the paint. Visual inspection of the tube through the jar wall indicates when there has been sufficient solvent action.

When the tube is removed, a towel or cleansing tissue may be used to wipe off the residue of the manufacturer's label intended for the pharmacist, and the prescription label is applied. The cap should be removed from the tube, Mr. O'Brien points out, to permit evaporation of any chloroform that may have seeped around the tube-threading for the cap.

Shorter Hours IN YOUR PHARMACY

by THEODORE H. McCOSH*

SHORTER hours of employment in pharmacy has come to be a timely and popular subject. It has been impressed upon the pharmacy owner by forces from two directions: by his own lengthened hours of service due to the wartime shortage of licensed employees, and by the pressure of gradually shortened hours of work offered employees in most other vocations.

Why is it so difficult to abandon the late night hours in retail pharmacy? Mainly because the tradition is so impressed upon the minds of those in the profession that they are unable to think in any other terms.

Of course the strain of long hours was not so severe in the days when plenty of pharmacists could be employed at low salaries. Pharmacy owners were not greatly interested in cutting hours of operation. The long hours frequently did not affect their lives, economic pressure was strong, and not too much thought was given the employee. When pharmacists became scarce, the employer had to work through the hours his pharmacy was open. Then he began to think how hard his lot was. And, in many instances because of failing health, he was forced to discontinue night operation.

A marked social trend in the field of labor is toward shorter working hours in all lines of trade and industry. The pharmacy employee naturally is not content to be an exception. He, too, is demanding sane working hours and will get them if he is to remain in pharmacy.

The long hours in the pharmacy became a major contributing factor to the lack of interest in pharmacy on the part of our young people. Although our colleges are crowded today, this factor will remain to discourage the right type of prospective pharmacist unless we keep step with social progress and offer reasonable hours of employment.

It has been proved beyond all doubt in my mind that discontinuing night operation of a pharmacy or drugstore does not necessarily decrease the volume of business nor the quality of service to the public. Just the reverse has occurred, in my experience.

I remember how I felt about this matter when I was pondering the question of closing our drugstore at 6:30 p. m. For fourteen years I had opened at 8 a. m. and closed at from 10 to 12 p. m. My patrons simply would not put up with this nonsense of early closing!

As time went on I was forced to adopt earlier closing hours because of ill health. Much to my surprise, people did not mind the idea of the drugstore closing. In fact, some remarked that it was the sensible thing to do. Volume did not drop even though I was the only one of nine drugstores to close evenings. Within six weeks, all drugstores in my community had voluntarily adopted the night closing, and in many towns throughout the country pharmacists later adopted shorter hours. I have not found one person, who has put evening closing into effect, who does not say it is the best thing that has happened to him in years, and that he hopes he never has to go back to slave hours. Sales volume usually has

* Pharmacist, Gering, Nebr.
Presented to the Section on Practical Pharmacy, AMERICAN PHARMACEUTICAL ASSOCIATION, 1947 meeting.

not decreased. This is not just my experience, but is the story of many.

The pharmacy employee is certainly in sympathy with this movement. In fact he is, in many instances, largely responsible for bringing it about. It is my prediction that pharmacists who do not favor this shorter-hours program will be forced to adopt it because of lack of assistants. This is a social trend and we must accept it.

The pharmacist has other responsibilities to consider besides continual professional service. He must always be alert to his job, which is not humanly possible if he works fourteen hours a day. This, in itself, can lead to disaster; only one serious error would far overshadow any extra service to the public he might render by longer hours.

There is no pharmacist who is not fully aware of his responsibility to public health. He is always willing to be called to his pharmacy after hours to render service if it is needed. But that does not mean that he has to remain there all hours of the day and night.

Pharmacists remind me somewhat of the cow pony which was trained to stand when the reins were dropped. He never knew any different and could not break away from his old custom. The reason the pony stands without being tied is because he never experienced what could happen if he broke away.

What makes you think so much more is expected from you by the folks in your town than is required of other types of professional and business men? They have for years made a success of their callings and have not been open every night and Sundays. Why do you think you cannot do the same?

The Pharmacist and His Family

The pharmacist and his family have always been somewhat of a problem, of which the outside world hears little. The pharmacist's wife and children rarely know him as other fathers are known to their families. Let me tell you my own experience.

I have three children, all born in our town. The two oldest, who are of high-school age, were born in my early days of retail pharmacy. I usually left home at 7:30 a. m., then rushed home again for meals, and finally closed at 11 p. m. So, this oldest son and daughter grew up. They were well along in school before I had time to know them. The youngest daughter was still a small child when I acquired saner hours. And I had time to read to her and to listen to her stories and experiences. We could sit down at night and she knew what it was to sit on my lap and experience the intimacy of parenthood which the two older ones never knew.

When you go home at night and sit down to read your paper before returning to the night shift, and that boy or girl stands around close by until you drop your paper and say: "What is it, son?" or "What is it, sister?" and they turn away and say: "Oh! Nothing, Dad," you think the younger generation is a queer lot. They are not. You are. It is you they want! There is something in the way of companionship and affection that is just not there. They find this only in the closeness of their mother.

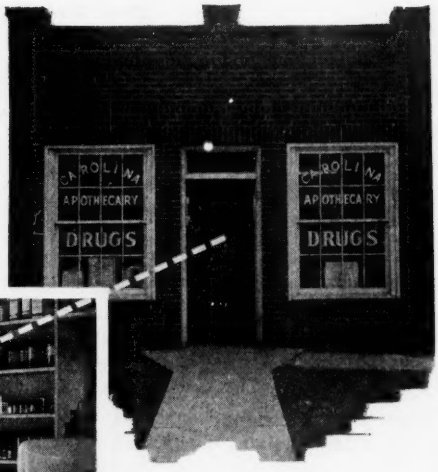
You, as a father, owe more to that boy or that girl that is yours than to anyone else in the world. And today, more than ever before in the history of this nation, youth is in need of guidance and of good parents. You owe it to them, and it is also your duty to share the responsibility with their mother, who also happens to be your wife. Sometimes pharmacists' families wonder if they have a husband and father.

Do not get the idea that, because you are going to close your pharmacy evenings, you are going to be idle during those hours. It will be only a short time until you discover the many things in your community that need your help. There will be new experiences for you and jobs that have been handled by others with which you, as a good citizen, should have been lending a hand. It is your duty, if you live in a democracy, and I think it is still considered such, to assume your share in making it work. There never was a time when it needed leadership more. Our communities and our country need men who have the understanding of human relations that you have. The opportunities that are waiting for you as a father and a citizen you will never know until you break away and try.

Many overworked pharmacists have died before the attainment of their life expectancy. Whatever the cause, did they either put into life or get out of it that which we have a right to expect? Was their one-track existence for gain? The graveyard is no place for a well-to-do pharmacist. Was it for service? The community will little recognize or appreciate it.

The remarks I have made I present as a plea. They deserve your most earnest thought. I am convinced that the general adoption of shorter hours. is entirely practical. By so doing you will profit more than you can conceive. Pharmacy should and I believe can offer a good livelihood without taking from us our place in the family and the community.

WHAT SHALL I STOCK?



by W. G. DUDLEY, JR.

CAROLINA APOTHECARY,
REIDSVILLE, N. C.

PUBLIC ACCEPTS FIRM POLICY IN PRESCRIPTION PHARMACY

WHAT to stock and what not to stock is an important question that faces the pharmacist attempting to open and operate an apothecary shop, or professional pharmacy. Our own experience with thi; problem may be of interest to other pharmacists. In a city of 10,000, with both proprietor and patrons familiar only with so-called "full-line drugstores," this largely resolved itself into setting up a policy and then educating the public to what is not stocked.

Our venture was launched in 1945 under the name "Carolina Apothecary," with a neon sign simply stating: *PRESCRIPTIONS—DRUGS.* There were six other drug outlets in town: four general drugstores, an industrial dispensary, and the hospital drug room. There were 13 physicians in the community, including three surgeons.

Initial promotion of the apothecary shop included proper announcement in the local paper, direct mail to all names in the telephone book and personal interviews with physicians. Since then, newspaper space has been used two or three times a month, and direct mail on every occasion that proper copy is available; prompt service both to the physician and patient is stressed *and* practiced.

Although no record was kept, we feel safe in saying that almost half the calls during the first two weeks were for neither drugs nor sickroom supplies. Ice cream, gum, candy, lotions, cosmetics of all kinds, tobaccos and numerous other sundry items were called for frequently. Potential patrons were referred to the proper sources for such items as courteously as is humanly possible.

Some appeared disgusted because our sign distinctly said "drugs"; others seemed a bit abashed at assuming we had the merchandise in question, while others just thanked us and left. That a large number of these patrons are willing to return for the professional services we do offer is indicated by our growing volume, which is satisfying from both personal and financial viewpoints.

Stock has been elaborated with our basic policy constantly in mind: A product must always be a drug, health item or sickroom necessity.

We have now added toothpaste, toothbrushes and oral antiseptics. At first we had no "patents." This policy was modified since physicians add orders for a well-known laxative or other household remedy on the bottom or back of prescriptions. In obtaining prescription refills patrons also frequently call for a household remedy, either with or without a physician's

recommendation. The result, of course, was addition of the most popular "patents," but only for service sales. There is no featuring, advertising or recommendation.

At the end of eighteen months of operation a record was kept of every sale for a week*, during which we had 426 patrons. Was it a new prescription? Refill? Was it for an item we did not stock? The results of this study are summarized in the accompanying table.

A patron with two new prescriptions is listed as one item, a patron with a new prescription and a refill is indicated as two items, or any number of prescriptions plus a product such as toothpaste are considered as two items. The classification reveals the relative volume in various categories of service. Most of these are self-explanatory, although several classes given in the table may be clarified as follows:

Hospital supplies: e.g., cotton, bandage, rubber goods, bed-pan, crutches, etc.

Nutritional: e.g., vitamins, powdered milk, protein hydrolysates, casein, etc.

Personal products: e.g., contraceptives, sanitary napkins, etc.

Baby accessories: e.g., nipples, bottles, oils, lotions, creams, powder, etc. (here we border on cosmetics).

* March 10 through 16, 1947.

We found that every 100 patrons ask for 115 items. The table shows, by the low number of unfilled orders, that our patrons now know what is stocked. It shows approximately two-thirds of our volume is new and refill prescriptions. In addition, over 20% of the total volume is dispensed from stock required to fill these prescriptions.

About 10%—represented by dental and personal products, "patents" and baby accessories—comes from other than prescription stock. We feel that these are necessary adjuncts to the welfare of the patient and the continued success of the shop.

Although the shop is a small enterprise, it has more than doubled the net income previously received as a salaried pharmacist. There is no indication that volume has reached its peak.

The problem of deciding what not to stock in establishing a prescription pharmacy has been pointed out. In meeting this problem successfully we have found it desirable, professionally and financially, to define the scope of our service and to respond to public demand only within the scope of that defined policy. In our experience the public as well as the medical profession will accept and respect specialized pharmaceutical service when the pharmacist's objectives are made clear through newspaper announcements, direct mail and courteous personal contacts.

FREQUENCY OF DEMAND FOR PRESCRIPTIONS AND HEALTH SUPPLIES DURING TYPICAL WEEK

	New Prescriptions	Prescription Refills	Pharmaceuticals by Name	Not Stocked	Sickroom Supplies	Dental	Nutritional	Personal Products	Patents	Baby Accessories	Ampuls	Ethical Proprietaries
Monday: Per 100 customers	37	32	8	2	5	1	4	1	4	4	5	8
Tuesday: Per 100 customers	50	22	4	..	2	3	6	3	7	3	4	11
Wednesday: Per 100 customers	66	31	3	4	8	5	..	8	5	8	5	11
Thursday: Per 100 customers	43	18	8	1	12	1	3	2	4	..	7	9
Friday: Per 100 customers	50	30	3	1	4	..	1	..	5	1	..	9
Saturday: Per 100 customers	51	31	4	..	3	..	..	2	7	..	..	11
Sunday: Per 100 customers	75	13	..	1	..	..	..	..	13	..	..	6

Science News Capsules

A SINGLE GIFT EYE can make two eyes with corneal defects see again. Dr. G. P. Landegger of Los Angeles, at the meeting of the American Academy of Ophthalmology and Otolaryngology, described the technique he used in transplanting only half of the cornea from a gift eye to the eye of each of two boys, restoring 20/20 vision in both.

SOLID CHUNKS OF GASOLINE are reported possible through research by a French chemist, who is now working for the U. S. Army. After first news of the project appeared in a French English-language newspaper in New York, an Army spokesman conceded that Chemist M. Pathus-Labour is developing his discovery in this country at the National Bureau of Standards. In addition to solid forms of gasoline that will burn but not explode, the chemist is said to have developed a non-inflammable film in which gasoline can be packaged and handled.

USE OF STREPTOMYCIN for one kind of vertigo typical of middle ear disturbance was reported from the meeting of the American Academy of Ophthalmology and Otolaryngology. Despite the fact that vertigo has occurred in some patients receiving streptomycin, Dr. E. P. Fowler, Jr., of New York found that the drug was helpful in some established cases of the disease. He warned against use of streptomycin for any patient with vertigo who is over 50 years old.

GLAUCOMA, a disease marked by intense intraocular pressure and often resulting in blindness, runs in families and in most cases follows the laws of heredity very closely, Drs. Adolph Posner and Abraham Schlossman of New York concluded in a study reported to the American Academy of Ophthalmology and Otolaryngology.

A BILLION ELECTRON VOLTS would be developed in an electron linear accelerator that has been planned from a model now operating. This new tool for probing the secrets of atoms will bring light energy on the order of cosmic rays into scientific laboratories. It was designed at Stanford University.

A MASTER HEARING AID can be made that need not be prescribed individually as now recommended and that will suit almost all deafened persons, according to a report from the Harvard Psycho-Acoustic Laboratory. "It is only a matter of time and continued research," says Dr. S. S. Stevens, "before a hearing aid is available which will meet all the demands imposed by most deafened ears. And with the improved fidelity in amplification will come new lightness, ruggedness and general economy."

SOUND TOO HIGH-PITCHED for the human ear to hear, produced by the ultrasonic siren, contains enough heat energy to light a pipe, pop corn, or kill a mouse. Details of the device and some of the biological effects that can be produced with it will soon be published in the *Journal of the Acoustical Society* by Dr. H. K. Schilling of the Penn State College acoustics laboratory. Possible practical uses include the sterilization of foods, medical treatments and surgery, treatment of seeds to increase germination, elimination of the smoke menace and speeding chemical reactions.

MOST VIOLENTLY RADIOACTIVE of the chemical elements, curium, has been isolated and seen for the first time by human eyes. This achievement was announced by Dr. Isadore Perlman of the University of California to the American Chemical Society. The element, number 96, is the most dangerous of all the elements to handle. Its isolation is considered one of chemistry's most difficult separations because of a similarity to americium, from which it was made by bombardment in the atomic pile.

NEW PERFUMES, FLAVORS AND DYES may be fashioned chemically from silicon, Drs. E. H. Weller and S. H. Bauer of Cornell University reported at the meeting of the American Chemical Society. An extensive study has been made of the "siloxane" ring, hexamethylcyclotrisiloxane, which holds the possibility of rivaling carbon in the making of ring compounds.

A NEW TYPE OF HEARING AID, utilizing a printed electronic circuit similar to that of the proximity fuze of World War II, has been developed by the Allen-Howe Electronics Corp., Peabody, Mass. Advantages claimed for the cigarette-package size unit are space-saving, cost-saving and reliability.

SMALLER DOSES of influenza virus vaccine may produce satisfactory immunity without the frequent untoward reactions observed with the present dosage, Dr. J. E. Salk of the University of Michigan School of Public Health reported at the meeting of the American Public Health Association. He found that most reactions were not due to impurities in the vaccine but to a dose higher than needed to give maximum protection. Until a practical procedure can be worked out to adjust dosage by estimating the variation in antibody response among indi-

viduals, a dose one-half or less of that now being used was recommended.

GEORGE W. MERCK has received the Chemical Industry Medal for 1947. The award was made by the American Section of the Society of Chemical Industry for Merck accomplishments in producing penicillin, streptomycin and other modern drugs.

EPIDEMIC INFANT DIARRHEA may be controlled by streptomycin. In the treatment of 17 infants, described in two reports by Army medical officers, streptomycin is credited with saving several lives and shortening the period of illness in other cases. The series was much too small to warrant conclusions, but further clinical studies were urged.

EUROPEAN POPULATION is now increasing faster than before World War II, even though millions are on the edge of starvation. At the end of another decade there will be 22,000,000 more mouths to feed in Europe, according to G. I. Burch, director of the Population Reference Bureau. In spite of the great loss of human lives in Europe caused by World War II, the population has increased 11,000,000 during the past decade.

STREPTOMYCIN PRICES may be further reduced through use of a new soybean nutrient medium. It is not only much cheaper than meat extract for this purpose, but is claimed to increase the yield.

A SPLEEN EXTRACT has apparently checked cancer in three patients treated at the Hahnemann Medical College and Hospital, Philadelphia. The extract, still in a highly experimental stage and not claimed to be a cure, will be studied further (*Science*, 106: 348, 1947).

AMERICANS OF THE FUTURE are being killed at the rate of more than 12 per 100,000 population each year by diseases that attack them before they are born. The causes of this loss of life, and the crippling among those who survive pre-birth damage, are "largely accidental and preventable," it was reported to the American Public Health Association.

SYNTHETIC PYRETHRUM SUBSTITUTES have been patented (No. 2,428,844) with rights assigned to the government. Any one of three easily prepared compounds was found to be an adequate substitute for imported pyrethrum or derris. They are: di-isopropyl acetamide, di-isobutyl acetamide and heptyl acetamide. Useful for quick knock-down effect, the chemicals may be used in combination with DDT, which provides a sure lethal action.

THE SIGN OF THE GOLDEN MORTAR was the symbol of a pharmacy (below), opened in 1853, in which William Sydney Porter and Lunsford Richardson of Greensboro, N. C., once practiced. Mr. Porter is the immortal "O. Henry" of literature; Mr. Richardson was noted in the South for his philanthropy, church work and for promoting better interracial relations, and in this pharmacy developed the line of products to become known under the trade name of "Vicks." Earlier, this same pharmacy was owned by "Will" Porter's uncle, and it was here that the man subsequently known as O. Henry received his training as a pharmacist.

This fall, on the 85th anniversary of the birth of O. Henry, the Greensboro Historical Museum Society dedicated a memorial room including a rare collection of O. Henryana and a re-created section of the old "Dr. Porter's Drugstore" (shown in the photograph).

PRESCRIPTION Information SERVICE

SUBMIT YOUR PROFESSIONAL PROBLEMS TO THIS JOURNAL, 2215 CONSTITUTION AVE., WASHINGTON 7, D. C., GIVING ALL PERTINENT DETAILS. SERVICE TO READERS IS PROVIDED BY THE A. PH. A. LIBRARY AND TECHNICAL STAFF AND THE FOLLOWING CONSULTING BOARD OF PHARMACEUTICAL SPECIALISTS.

MAISON DE NAVARRE
LOUIS FISCHER
LOUIS GERSHENFELD
MELVIN W. GREEN
ALBERT P. LAUVE
ADLEY B. NICHOLS
GEORGE C. SCHICKS
GEORGE L. WEBSTER
LEROY WEIDLE
LOUIS C. ZOPF

FORMULA FOR BURN DEBRIDEMENT

Kindly forward sources of powdered phosphoric acid, powdered pyruvic acid and Methyl Parasept. The physician's reference for the preparation desired is Annals of Surgery, 125: 427, 1947. He refers to the phosphoric acid as a powder; could the U. S. P. product be intended?—H. B., Pennsylvania

Pyruvic acid may be obtained from such firms as Eimer and Amend, 635 Greenwich St., New York 14, and the Paragon Testing Laboratories, 345 Henry St., Orange, N. J. Methyl Parasept is the trade name of the Heyden Chemical Corp., 50 Union Square, New York 3, for methyl parahydroxybenzoate. This is recognized in U. S. P. XIII under the name methylparaben.

The paper in the April issue of *Annals of Surgery* refers to readily wetted powders for the formation of acid-containing ointments, used for debridement of burns. Phosphoric acid U. S. P. is used in the formulations. The September, 1946, *Scientific Edition* of our JOURNAL (35: 275, 1946) contains a paper describing the development of these preparations and gives working directions for making the powders.

WHAT IS SECRETIN?

We have been asked to obtain a supply of secretin. Would you send us the available information concerning this item?—A. S., Kansas

Although secretin has been used as a general term for any hormone that stimulates glandular secretion, it has come to refer specifically to a hormone secreted in the duodenum and jejunum and associated with pancreatic secretion. It may be obtained as a purified extract of the lining of the intestines but to our knowledge secretin is not commercially available. We understand that Friedman and Snapp have published on secretin recently in the *Proceedings of the Physiological Society of Pennsylvania.* We would suggest that you contact Dr. M. H. Friedman at Jefferson Medical College, Philadelphia, Pa., who will probably be able to advise you concerning current work with this substance and any sources of supply.

ACACIA OR BENTONITE INDICATED

I would like your opinion on the technique and method of compounding the following prescription that we received from a dermatologist:

Zinc sulfate	2
Pot. sulfurat	2
Calamine	6
Boric acid	4
Glycerin	2
Witch hazel	30
Rose water, q. s.	180

Sig. External use two or three times daily.

The method that was used in our pharmacy was as follows:

1. Dissolve the zinc sulfate in 15 cc. rose water and filter.

2. Dissolve the sulfurated potash in 15 cc. rose water and filter.

3. Add the sulfurated potash solution slowly

to the zinc sulfate solution while continually stirring.

4. Dissolve boric acid in 100 cc. of rose water, heat in water bath until dissolved, and then allow to cool.

5. Add the glycerin to the calamine in the mortar and cleanse from mortar with the boric acid solution. Add witch hazel slowly.

6. Add solution of step #5 to sulfurated potash solution and dilute with rose water to 180 cc., shaking well.

This method produces a mixture that readily settles out of solution. Could this method be improved without changing the prescription?—F. C., Vermont

We see no reason why the prescription cannot be filled in the manner you suggest. The prescription will contain a large quantity of sediment, which must be shaken prior to use, but this is intended.

If you are interested in holding the material in suspension better, use either bentonite magma or mucilage of acacia. Our experience shows that it takes about 30 or 40 cc. of bentonite magma or about 10 cc. of mucilage of acacia. The acacia appears to hold the suspension somewhat better but does not give the prescription the spreading qualities of bentonite.

COAL TAR INCOMPATIBILITY

How can the following prescription be filled to give the right kind of smooth, clean ointment?

Coal tar
Zinc oxide, aa..... *drs. ss*
Vaseline..... *ozs. ii*

Mix

The tar will not dissolve in the Vaseline and leaves small flakes in the finished product.—B. E., Arkansas

Coal tar is incompatible with the petrolatum. There are two ways in which this can be obviated. Note that coal tar ointment, U. S. P. does not materially differ from your prescription except that it contains a slightly different quantity of coal tar and, in addition, starch. If it were agreeable to the physician to use the official prescription, you would have no difficulty. Incorporation of the zinc oxide and the starch with the white petrolatum forms a smooth primary paste that will enable the coal tar to mix very well. If this change is objectionable to the physician, however, we have found the following plan to be helpful:

To 5 parts of glycerin add 2½ parts of coal tar and make a paste. To 5 parts of zinc oxide and 5 parts of glycerin add the remaining 2½ parts of coal tar and mix well. Incorporate most of the petrolatum with the glycerin-coal tar paste. Incorporate the zinc oxide-glycerin-coal tar paste; mix well and add the remaining petrolatum.

SEPARATE PRESCRIPTIONS BEST

Could you tell me why the following prescription changes color after a short while?

Phenobarbital..... *gr.* ½
Papaverine HCl..... *gr.* ½
Aminophylline..... *gr. iii*
Acid acetylsalicylic..... *gr. v*
To make into 60 capsules.

—M. A., Pennsylvania

The aminophylline and acetylsalicylic acid apparently react, causing the prescription to darken and become somewhat moist. Our suggestion would be that the physician prescribe aspirin in a separate capsule, or in tablets. The use of magnesium oxide is often indicated in mixtures which become moist, but we hesitate to use it in this instance because of its possible neutralizing effect on the ingredients. It is quite possible that the material could be diluted with some dry starch, adding a portion to the acetylsalicylic acid, and another portion to the other ingredients, and mixing the two without excessive trituration. However, the capsule is already a large one, and additional material will undoubtedly make the capsule too large. Suggesting that the aspirin be dispensed separately is probably best.

DMELCOS VACCINE

Please send me available information about Dmelcos Vaccine. Why is it not available in this country?—B. P., Pennsylvania

It is our understanding that Dmelcos Vaccine is made from Ducrey's bacillus and is used in the treatment of chancroids. No vaccine may be imported into this country unless the firm making it is licensed with the United States government.

LITERATURE ON VITAMINS

Please tell me where I may obtain the latest books on vitamins.—N. G., Athens, Greece

Several volumes pertaining to vitamins are

as follows: Eddy and Dalldorf, *The Avitaminoses*, published by The Williams & Wilkins Co., Mt. Royal & Guilford Sts., Baltimore; Franklin Bicknell and Frederick Prescott, *Vitamins in Medicine*, published by William Heinemann, Ltd., 99 Great Russell St., London; H. R. Rosenberg, *Chemistry and Physiology of the Vitamins*, published by Interscience Publishers, Inc., New York.

WATER CONTENT IS TOO HIGH

Would appreciate your comment on the best method of preparing the following prescription, used as a liquid to be rubbed into the scalp:

Menthol	*0.5*
Lenigallol	*5.0*
Ol. ricini	*30.0*
Alcohol 70%, q. s.	*120.0*

The doctor said it was permissible to use rubbing alcohol (ethyl) to reduce the price of the prescription.—W. M., New York

We believe that the difficulty is the use of 70% alcohol. There is sufficient water present to interfere with the solution of the castor oil and other ingredients. We suggest that U. S. P. 95% alcohol be used. It may be necessary for the prescriber to cut the castor oil content somewhat.

REMOVING CIGARETTE STAINS

What could be used as an effective means of removing cigarette stains from the fingers?—B. F., Pennsylvania

The *Chemical Formulary* by H. Bennett gives the following procedure for cigarette stain removal.

A.	Potassium permanganate solution	2%
B.	Sodium bisulfite	10
	Orris root, powdered	10
	Perfume, to suit	

Apply solution "A" with a swab and after a few minutes rub with "B," moistening with water if necessary. Wash well with soap and water.

NON-FOAMING WETTING AGENT

Can you advise us concerning a non-foaming wetting agent that can be used in internal pharmaceutical preparations?—N. S., New Jersey

To our knowledge no wetting agents are completely free from foaming characteristics. The basic principle by which wetting agents act is to lower the surface tension and this action is responsible for foaming. However, some wetting agents produce more foaming than others. It is our impression that the Spans and Tweens have a minimum of foam-producing activity. Many of these agents are sufficiently free from toxicity to be used in foodstuffs and therefore would be satisfactory for internal preparations.

It would not be possible for us to judge which one of these series of compounds would be most adaptable for your purpose, but the manufacturer will no doubt help you select the proper agent for your needs. These compounds are made by the Atlas Powder Company, Wilmington, Del.

SCHLESINGER'S SOLUTION

Can you supply us with the formula for Schlesinger's Solution? It is a narcotic and is usually prescribed in 10- or 15-drop doses.—G. M., Ohio

The formula for Schlesinger's Solution, given in *Pharmaceutical Recipe Book III*, page 214, is as follows:

Scopolamine hydrobromide	0.25	Gm.
Morphine hydrochloride	20	Gm.
Ethylmorphine hydrochloride	40	Gm.
Ampul water, a sufficient quantity,		
To make	1000	cc.

Dissolve, filter and sterilize by Process F (N. F. VIII, p. 753).

REPLACEMENT FOR "FIBROLYSIN"

We understand that Merck no longer manufactures "Fibrolysin." As one of our leading ophthalmologists uses this solution with equal parts of normal saline solution as "eye drops," we expect a request from him for a similar solution.

Would you oblige us with a thiosinamine and sodium salicylate stock solution formula that will be stable for a month or less; also the best method for sterilizing this solution.—G. B., Louisiana

Fibrolysin is said to be a 15% solution of a mixture of thiosinamine and sodium salicylate. The mixture is stated to comprise 2 mol. of thiosinamine to 1 mol. of sodium salicylate. This would be approximately an 8.8% solution of thiosinamine and 6.2% of sodium salicylate.

Such solutions are said to be unstable. Therefore the use of heat in sterilization should be avoided. We would suggest that the solution be prepared under aseptic conditions, followed by filtration through a bacteriological filter and stored under sterile conditions. The solution probably should not be stored for a long period of time.

NOVAK'S SOLUTION

Please give me a formula for Novak's Solution. —I. M., Colorado

The formula for preparing Novak's Solution is as follows:

Alcohol, 95%	525.0
Acetone	100.0
Distilled water	375.0
Cresol, U. S. P.	5.0
Mercury bichloride	0.7
Eosin Y	0.6
Acid fuchsin	0.08

BUFFERING PARENTERAL CITRATE

We would like to know how to buffer intravenous solution sodium citrate. Also what should be the final pH of intravenous solution of sodium thiosulfate?—B. F., California

According to Loutit, Mollison and Young (*Quarterly Journal of Experimental Physiology*, 32: 183, 1943) sodium citrate is buffered by the use of enough citric acid to produce what is apparently disodium citrate. Dextrose is also used and the following formula is recommended:

Citric acid	0.5875 Gm.
Trisodium citrate ($2H_2O$)	1.6600 Gm.
Dextrose	3.7500 Gm.
Distilled water, *q. s. ad*	125.00

The authors claim that the advantage of such a solution is that during autoclaving no carmelization takes place and that red cells survive better.

Solutions of sodium thiosulfate should have a final *p*H of about 7.5 according to *Remington's Practice of Pharmacy*. Because distilled water is too acid it is customary to boil the water before making the solution.

OINTMENT BASE FOR ACETATE

I have a prescription calling for 24 drams lead acetate to be made into a 1-lb. water-soluble ointment. What would you suggest that I use?—B. E., New York

We would suggest hydrophilic ointment U. S. P. XIII for incorporating the lead acetate. This will be found on page 351 of the new U. S. P.

If an ointment prepared with this base is too stiff a small amount of water may be incorporated. An ointment prepared with this base has been stable for a week in our laboratory and shows no sign of deterioration.

—R—

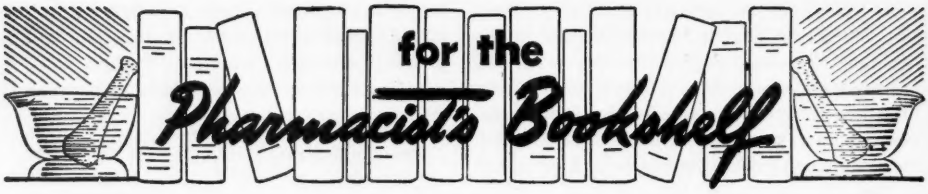
SECRETARY FISCHELIS VISITS WEST COAST

DR. ROBERT P. Fischelis, secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION, has returned from the West Coast where he developed plans for the 1948 convention in San Francisco and inspected Army and Navy hospitals, with regard to pharmacy, as a civilian consultant to the Medical Departments of the armed forces.

Dr. Fischelis was appointed an honorary consultant by the Secretary of the Navy to cooperate with the Chief of the Bureau of Medicine and Surgery "in the solution of important and imperative problems affecting the health of Navy personnel." The A. PH. A. secretary is one of 17 consultants serving in this capacity from various fields. Only one other consultant, Dr. Charles Sheard of the Mayo Clinic (optometry), is a non-medical man. In the Army, Dr. Fischelis is one of a panel of civilian pharmacy consultants named in connection with establishment of the Medical Service Corps.

Dr. Fischelis was requested by the Army and Navy to review operation of the pharmacies and related facilities in service hospitals in California. His suggestions based on this tour of inspection will be utilized in connection with regulations being prepared on the new Corps in the Army and Navy.

During his trip, Dr. Fischelis laid the groundwork for the San Francisco A. PH. A. convention to be held the week of August 8, 1948. He also visited local branches of the A. PH. A. at Los Angeles and San Francisco, addressing the latter branch at its October session, and also addressed the student branches at the University of California and the University of Southern California.



A few books are considered below, published during 1946 or 1947, which seem particularly suitable as gifts for members of the health professions or for the pharmacist's perusal on a winter's night off duty.

EPITOME OF THE U. S. P. AND N. F.

The *Epitome of the Pharmacopœia and National Formulary* has made a place for itself, primarily among physicians, because it brings together in compact, ready-reference form the essential information needed in prescribing official drugs. The eighth edition just issued covers the new U. S. P. XIII and N. F. VIII. Preparations are grouped under each basic drug, and for each item are listed: official titles, synonyms, brief definition, physical properties, actions, uses and dosage.

The volume is published under the supervision of the A. M. A.'s Council on Pharmacy and Chemistry. In accord with the Council's policy for all its publications, official doses are given only in the metric system. The comments under "Uses" represent critical therapeutic evaluations in concise form.

This should represent an ideal gift from the pharmacist who wants to start the New Year off on a cordial note with his medical acquaintances.

EPITOME OF THE PHARMACOPŒIA AND NATIONAL FORMULARY—Council on Pharmacy and Chemistry—*J. B. Lippincott Co.*, Philadelphia, Pa.; 238 pp., $2.

FROM THE PAST, A STIMULUS FOR THE FUTURE

The significance of George Urdang's book issued last year will be as timeless as the service of the pharmaceutical profession he portrays. *Pharmacy's Part in Society* proves to be an impressive part indeed when its scattered fragments are unified in such a scholarly and convincing manner. Against the broad background of social and scientific development through the centuries, Dr. Urdang silhouettes the contributions that pharmacists have made in human endeavor: within the profession, to public health, to the sciences, industry and education, and to general culture.

This book is not a history. It is an inspiring account of pharmacy's place in the local and world community. It should be a welcome gift to members of the profession—a stimulus to renewed confidence in the significance of their work and their profession during the New Year and years ahead.

The author, now director of the American Institute of the History of Pharmacy at the University of Wisconsin, is one of the few pharmacists designated as honorary members of the AMERICAN PHARMACEUTICAL ASSOCIATION. This reflects the general recognition of his eminent place as an interpreter and recorder of pharmacy's history.

Dr. Urdang's account of pharmacy's part in society has a thought-provoking foreward written by Robert P. Fischelis, secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION.

PHARMACY'S PART IN SOCIETY—George Urdang—*American Institute of the History of Pharmacy*, University of Wisconsin, Madison, Wis.; 93 pp., illus., $5.

A SELECTED LIST OF ESSENTIAL DRUGS

Useful Drugs represents an attempt to provide the medical student or practitioner with a selective list of essential drugs together with the basic information needed for prescribing. In compiling the volume, all official drugs and the unofficial drugs represented in N. N. R. are put through a winnowing and sifting process. The resulting compilation encourages rational therapeutics by giving the practitioner a reference source for medication of "general sufficiency" without it being necessary for him to make his own evaluation and selection from many drugs offered for the same therapeutic indications.

Useful Drugs is issued under the direction and supervision of the Council on Pharmacy and Chemistry of the American Medical Association. The new fourteenth edition is based on U. S. P. XIII, N. F. VIII and N. N. R. 1947.

For each medication selected for inclusion there is given a description and statement of properties, followed by a discussion of actions, uses and dosage that is somewhat more extensive than that appearing in the *Epitome of the U. S. P. and N. F.* Classes of medications, such as the estrogens, are grouped under more detailed general discussions.

USEFUL DRUGS—Council on Pharmacy and Chemistry—*J. B. Lippincott Co.*, Philadelphia, Pa.; 241 pp., $2.

THE SUBTLE SENSE

The pharmacist's sense of smell is probably more highly developed than that of ordinary folk; his nose becomes attuned over the years to the distinctive odors—subtle and otherwise—of the drugs and chemicals that he handles. Thus perhaps it is not so unusual that *The Subtle Sense* should have been writ-

ten by a pharmacist, albeit an unusual one who has a special way with words and odors.

Ralph Bienfang's book received favorable press comment when first issued last year and should be enjoyable to pharmacist and layman alike. The author has used considerable imagination, as well as a vast store of facts and suppositions, in putting together a sprightly volume on odors. This is reflected by a sampling of the intriguing chapter headings: The Physiology of Odor, Odor in Environment, Odor in Society, Odor as a Warning, The Business of Odors, Nostalgia Through Odors and Odor and Literature. Dr. Bienfang also ventures a chapter on The Future of Odor.

If the author becomes obtrusively enthusiastic about his subject at times, he may be forgiven; for he puts us in touch with both the significance and entertaining possibilities of something as elusive as the wind.

Dr. Bienfang serves as professor of pharmacy at the University of Oklahoma, and incidentally has been a member of the A.PH.A. for many years. His unusual avocation, the study of odors, led to his being consulted professionally on the subject by industrial concerns and to his appearance in Universal News Reel's "Stranger than Fiction" series.

THE SUBTLE SENSE—Ralph Bienfang—*University of Oklahoma Press*, Norman, Okla.; 157 pp., $2.

NEW AND NONOFFICIAL REMEDIES

The stature and influence of the work of the A. M. A.'s Council on Pharmacy and Chemistry is well recognized by practicing pharmacists and pharmaceutical manufacturers, as well as by the medical profession. In fact the Council's principal publication, *New and Nonofficial Remedies*, must be considered essential by every pharmacist.

The edition recently issued covers medicinal products evaluated and accepted by the Council up to January 1, 1947. Products admitted since that time have been described for pharmacists each month in THIS JOURNAL and may be consulted by reference to the annual index in this issue under "American Medical Association." As customary in N. N. R., drugs are grouped according to therapeutic classes. Each drug or closely related group of drugs is discussed in a general article, followed by the name, description and source of commercially available accepted products. Segregating the tests and standards for accepted products in a separate section represents a new departure in style.

Even at the higher price, N. N. R. remains a "best buy" for either the pharmacist or physician.

NEW AND NONOFFICIAL REMEDIES 1947—Council on Pharmacy and Chemistry—*J. B. Lippincott Co.*, Philadelphia, Pa.; 749 pp., $3.

DEAN WULLING, A.PH.A. PAST PRESIDENT, DIES

FREDERICK J. WULLING, dean emeritus and founder of the Minnesota College of Pharmacy and senior past president of the AMERICAN PHARMACEUTICAL ASSOCIATION, died on October 21 at the age of eighty.

He established the College in 1892, becoming dean when only twenty-five years old. He became dean emeritus in 1936. During the intervening forty-four years Dean Wulling placed his institution among the leaders in pharmaceutical education and he himself became a leader in the progress of pharmacy, not only in Minnesota but nationally. He had been a member of the A. PH. A. since 1893.

Frederick J. Wulling was born in New York City on Christmas eve, 1866. There, and in New Jersey, he received education in business, music, medicine and pharmacy. He became a licensed pharmacist after graduating with highest honors from the College of Pharmacy now affiliated with Columbia University. During the summers of 1887 and 1889 Dean Wulling conducted medical and pharmaceutical research in Europe. He held several teaching posts at the New York college and concurrently served as assistant editor of the *Pharmaceutical Record*.

After assuming the deanship at Minnesota Dean Wulling became active in developing the Minnesota State Pharmaceutical Association, maintained close liaison between practicing pharmacists and the College, and established in 1904 a Scientific and Practical Section of the state association, the first of its kind. He personally presided over the sessions of the Section until his retirement in 1936. Minnesota pharmacists amended the constitution of their association to establish for him the post of honorary president.

Over the years he held many national posts, including the presidency of this ASSOCIATION and of the American Association of Colleges of Pharmacy. He had also been a member of the U. S. P. Board of Trustees. Among numerous honors bestowed upon him were honorary degrees from Columbia University and the Philadelphia College of Pharmacy and Science.

ADR

DENTAL REMEDIES RECENTLY ACCEPTED BY A. D. A. COUNCIL ON DENTAL THERAPEUTICS

EPINEPHRINE AND RELATED SUBSTANCES

Epinephrine Injection, U. S. P. 1:1,000—Durst: Each cubic centimeter is stated to contain epinephrine (as hydrochloride), 0.001 Gm.; sodium chloride, 0.009 Gm.; sodium bisulfite, 0.0015 Gm.; chlorobutanol (chloroform derivative), 0.0035 Gm.; water for injection, *q. s.*

Distributed by S. F. Durst & Co., Philadelphia.

SODIUM SALTS

Normal Saline Solution—Durst: A brand of Isotonic Sodium Chloride Solution, U. S. P.

Distributed by S. F. Durst & Co., Philadelphia.

PENICILLIN

Penicillin Troches—Bristol: Each troche is stated to contain granulated cane sugar, 11 gr.; precipitated chalk, 2.1 gr.; talc, 0.7 gr.; magnesium stearate, 0.15 gr.; calcium penicillin G, 1200 units, and oil of peppermint, $^1/_{20}$ minim. In bottles of 20.

Manufactured by Bristol Laboratories, Inc., Syracuse, N. Y.

COUNCIL REPORTS

NEW POLICY ON DENTIFRICES

The Council on Dental Therapeutics of the American Dental Association has been an outstanding pioneer and influence in the evaluation and improvement of dentifrices for seventeen years. In 1930, when the Council initiated its program, the need for impartial and scientific standards in the field of dentifrices was acute. The Council, by establishing standards for composition, by delineating the claims which could be made and by encouraging the use of acceptable dentifrices, has made substantial contributions to oral and public health. Largely as a result of the efforts of the Council, therefore, most of the dentifrices available today are relatively safe for daily use.

In view of the distinct advances that have already been made and in keeping with its policy of constantly revising its program in order to reflect current professional and scientific opinion, the Council on Dental Therapeutics has concluded that additional progress can be made more rapidly by placing maximum emphasis on other phases of its long-range program regarding dentifrices. In order to accomplish such progress, the Council will discontinue the consideration of cleansing dentifrices with a view to their acceptance. The Council, however, will continue to evaluate such products and to encourage sound formulation and honest claims in order to advance the improvements that have already been made. In the future, too, the Council will give particular attention to dentifrices for which therapeutic claims are made, since the development of new drugs makes the appearance of many new products in this field quite probable.

The decision to discontinue the consideration of cleansing dentifrices with a view to their acceptance was taken by the Council after a serious study of all conditions in this area of its work. Cleansing dentifrices are essentially scouring agents, and this function can be performed quite satisfactorily for most people with a mixture of finely powdered salt and baking soda. As a result, the Council did not feel that the granting of a Seal of Acceptance would continue to have the same value in the field of dentifrices that it does in the more important fields of local anesthetics and other dental therapeutic agents.

The unsound and undignified advertising claims so frequently made in this highly competitive and commercial field will, no doubt, continue to be of concern to both the public and the profession. The increasing vigilance of the two Federal agencies concerned with such products and their claims should eventually insure proper safeguards through formal governmental action. The Federal Trade Commission, the Food and Drug Administration and state and local health departments should be urged by all members of the dental profession to continue to surround dentifrices with the safeguards necessary to public health.

Under this extension of its program, the Council on Dental Therapeutics, although not accepting cleansing dentifrices for inclusion in Accepted Dental Remedies, will continue to examine them routinely and will publish reports of its findings as conditions warrant. The annual report on "The Status of Dentifrices," published by the Council, will be continued and will contain data on the composition of the more widely used cleansing dentifrices and comments on the claims made for them.

The educational program of the Council will be expanded. Literature on dentifrices, toothbrushes and mouthwashes will be prepared and distributed without charge. Reprints of Council articles and other material will be available on request to the Council. Cooperation with governmental, professional and consumer agencies will be maintained as in the past.

Under this program, the Council hopes to be able to give increased attention to other products within its scope for which the development of scientific data and standards also will be highly significant. Thus the many products which compete for the dentist's attention, often on the sole basis of the art of the advertising writer, will have less chance for survival if they do not lead directly to the welfare of the patient.

Typical Days

FROM THE SECRETARY'S OCTOBER DIARY

—1st—

AN unexpected meeting on Pennsylvania Avenue with Ted Klumpp, Winthrop president, who has advanced ideas about cooperation between medicine and pharmacy to the benefit of both. In the afternoon a visit from Mark Merrell who is engaged in export promotion of antibiotics at the moment. A dinner conference with Council Chairman Beal at the Occidental, which continued far into the night at the Washington Hotel and covered all current A. PH. A. problems.

—2nd—

The day's heavy schedule pleasantly broken at noon conversing with George Archambault on problems of the U. S. Public Health Service whose hospital pharmacy division he heads. Given a little time and the necessary personnel, George will take the pharmaceutical services of the U. S. Public Health Service in the direction of high accomplishment.

—3rd—

Among the visitors today was Mrs. Rogers of Omaha, another one of the enthusiastic hospital pharmacists of the Middle West. Spent considerable time arranging for a news letter to the pharmacists of South America by way of a Pan-American scientific program sponsored by the Committee on Inter-American Scientific Publication. Glad to receive a telephone report from Troy Daniels in San Francisco denoting substantial progress on the arrangements for the 1948 convention.

—6th—

After a week end at Red Bank encountered the customary heavy Monday morning mail plus a series of telephone calls from Oregon, Illinois, Florida, West Virginia and way stations. Late at the office preparing JOURNAL copy which was overdue but caught the midnight mail.

—7th and 8th—

These days combining office routine with attendance at most of the sessions of the Pharmaceutical Survey Advisory Committee meeting at the Statler. Committee discussions are reaching the point where important decisions are in order, based on data assembled from various sources. Here the experienced mind and hand of Director Elliott and the smooth steering of the debate by Chairman Charters are manifest. And there was much significance in the remark of Dr. Charters who, like the Director, is a retired educator, when he said, "Never retire, for they will work you to death."

Throughout the discussion it was emphasized that planning for implementation of the findings and recommendations is an important factor of the Survey. Progress in this direction is evident, and the A. PH. A. is alert to its responsibilities in this phase of the undertaking.

Interesting phases of such meetings are the opportunities afforded to confer with men like Doerr, Walgreen, Beal, Swain, Taylor, Frailey, Clarke and others. Late in the afternoon and early evening riding with Don Clarke and Gloria Niemeyer to the airport, discussing Hospital Pharmacy Division programs and seeing Don safely on the plane to New York after a hasty meal.

—9th—

A pleasant visit with Army Deputy Surgeon-General Armstrong and Medical Service Corps Chief Colonel Goriup at the Pentagon discussing plans for inspection visits to Army hospital pharmacies at Walter Reed, McCornack and Letterman, in D. C., Pasadena and San Francisco respectively.

—10th—

Lecturing to the pharmacy seniors at George Washington University for two hours this day on pharmaceutical organizations and found the young men and women deeply interested in what makes pharmacy and the drug industry tick. At luncheon with Dr. Connor and Mr. Auk of the American Heart Association discussing pharmacy cooperation in the campaign to emphasize the importance of early diagnosis and prompt treatment of cardiac ailments. Next to the Walter Reed Hospital visiting the pharmacy and chatting with Maj. Zolenas and Lt. Cooper, both pharmacists, who have worked out an excellent service with the medical staff. And now some last minute chores at the office in preparation for the trip to the west coast.

—11th—

Some feverish activity at the office including a frantic search for a misplaced brief case, which turned up exactly where it had been left the day before. After final approval of the election bulletin and last minute instructions for handling a multitude of anticipated activities in the next ten days, off on the "Capital Limited" for Chicago, meeting John MacCartney of Parke, Davis and Company who was also enroute to the N. A. R. D. convention.

—12th—

The B. & O. on time as usual and the Sherman Hotel ready with its reservation, so off to a good start for the first N. A. R. D. convention in five years. At breakfast with Alabama's Gibbs, Watkins, Little and Alley. While waiting in line to register for the convention and receive the ticket which did not win the Packard, exchanged greetings with Moulton, Noh, Gnerich, Alice Esther Garvin and many others. The Lambert party at the Morrison was well attended.

—13th—

Breakfast with Al Fritz of Indianapolis who always has interesting and thoughtful comment on

pharmacy's difficult problems. Browsing through the drug show for a preview. It looks bigger and better than ever.

All the afternoon at the College of Pharmacy of the University of Illinois, meeting with the Policy Committee of the Hospital Pharmacy Division going over the program of hospital pharmacy projects for the coming year. In attendance were Dean Serles, Francke, Hansen, Zugich, Evlyn Gray Scott, Sister Clara Francis and R. P. F. All felt that much progress has been made but the full-time director is the key to future accomplishment.

A good dinner at Henrici's with a large delegation from Alabama, and then to the reception for President and Mrs. Otto Kohl; finishing a busy day in the quarters of Joe Noh who ably represents Winthrop as vice-president and knows how to entertain.

—14th—

Joining Swain and Costello for breakfast and then to the opening session of the N. A. R. D. convention, where all the officers made significant reports of progress and President Kohl was generous in his comment on A. PH. A.-N. A. R. D. cooperation. Touring the drug show booths with Bob Swain and picking up supplies of this and that sufficient to keep the teeth brushed, the face shaved and the acid stomach neutralized for months to come. At the afternoon session Carl Durham, Leslie Ohmart, Bert Mull and E. L. Newcomb performed notably.

—15th—

Early at breakfast with the Dixie Sunrisers who turned out in full force and were entertained by the wit and repartee of Chairman Dick Richards of Florida, who knows how to spark any kind of a meeting. Busy at the job of catching up with the mail from Washington and keeping the telephone wires hot until lunch time.

After listening to Attorney General Tom Clark's speech, a special session on A. PH. A. affairs with President Dretzka and ex-president Serles. Later an executive session with the president to review committee appointments and other current business.

—16th, 17th, 18th—

A breakfast conference with Nebraska's President Lindberg and Secretary Cora Mae Briggs on matters pertaining to their convention. Next a conference with Dal Bruner on pharmaceutical affairs in Iowa.

At high noon on the Santa Fe "Chief" leaving Chicago for Los Angeles. A pleasant ten-minute chat with Dean Bowers of the University of New Mexico at Albuquerque from the time the train pulled in until it left. Arrived on time Saturday morning at Los Angeles. The Biltmore Hotel has lost none of its charm.

An interesting conference with Dr. Walter Clarke, director of the American Social Hygiene Association, who is making a V. D. survey of this great city and pleased to have him report that pharmacy's record of cooperation is good. Now for a quick trip to Long Beach to inspect the U. S. Naval Hospital pharmacy where Capt. Hill and Lt. Stevens were hosts.

Next to the Jonathan Club at L. A. for a sumptuous dinner arranged by Dean Hall and associates with officers of the California Branch of the A. PH. A. and a distinguished group of professional pharmacists, including life member Orazio Tocco and Mrs. Tocco who are old New Jersey friends.

—19th—

Most of this Sunday catching up with the Washington mail and working on speeches for delivery in person and in absentia at various places during the coming week.

—20th—

Early on the way by motor to Pasadena for a visit to McCornack Hospital of the U. S. Army and found Col. Welch, the C. O., an old friend of student days in Philadelphia. The hospital pharmacy in charge of Captain Gordon was all that a hospital pharmacy should be. Now for an unscheduled visit to Cal-Tech's guided missile laboratory with Anthony Tocco as pilot and saw a number of German engines of destruction recovered from World War II and many U. S. developments in the experimental stage.

Next to address pharmacy classes of the University of Southern California on the campus of that rapidly growing institution. From there to see the "world's largest drug store" and the newly completed executive offices and experimental laboratories of the Rexall Drug Co., meeting Messrs. Davis, Hailer, Baker and others of the executive staff but missing President Justin Dart who was out of town. Late in the afternoon to the offices of the California Ph. A. and Southern California R. D. A. where Secretaries McCracken and Baird had kindly waited to discuss mutual problems. Just enough time left for the signing of important mail, a quick dinner and taxi ride to the L. A. station, boarding "The Lark" for an overnight ride to San Francisco.

—21st—

Greeted by Harry Hind as "The Lark" pulled into S. F. terminal on time. A quick ride to the Fairmont Hotel at the top of the hill from where one can catch the beauty of the setting which contributes to the charm of San Francisco. Sunshine and a clear sky, with visibility unimpaired, makes this a day to be remembered. Now came Troy Daniels and Miss Cooley of the S. F. Convention Bureau to join us in viewing the meeting room facilities at the Fairmont, and the Mark Hopkins across the street. After luncheon a further inspection of hotel facilities at the bottom of the hill and in the center of things. It all adds up to plenty of rooms and some excellent meeting facilities but not under one roof.

In the evening came the key men of San Francisco's drug industry and leaders in the pharmaceutical profession including the Board of Pharmacy, to meet at dinner and to discuss the plans for the A. PH. A. convention next August. Their unanimous choice for convention chairman is the justly popular and capable Dean Daniels of University of California College of Pharmacy, who presided, but who hesitates to assume the permanent task of keep-

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ing things moving. An enthusiastic gathering of capable men who will produce a fine convention.

—22nd—

Aroused from deep slumber at 6:30 a. m. by a telephone call from Washington where the clocks had already reached 9:30. Also much mail from various points requiring attention. Now in the company of Captain Street, pharmacy officer, motoring to Letterman Hospital for a view of the pharmacy and chats with medical officers and other personnel. Happy to welcome and be welcomed by Surgeon General Bliss, just in from Hawaii on the last leg of his tour of the Pacific areas where U. S. troops are stationed. Found him enthusiastic about developments in Army medicine and alert to the possibilities of the Medical Service Corps under Col. Goriup. After luncheon, off by automobile to Mare Island to view the Navy Hospital pharmacy there. A beautiful view of San Francisco harbor and environs en route. Captain Ross and the Navy medical staff extended every courtesy, and the pharmacy is well stocked and managed. After being safely delivered at the Fairmont by the Navy, took off for dinner at Joe DiMaggio's restaurant with Daniels, Hind, Affleck, Walsh and other Board of Pharmacy members. Next to address the A. PH. A. Northern California Branch, and ending a busy day with Harry Hind at the "top of the Mark" from where one can really see the city at night and marvel at the combined efforts of man and nature in producing a veritable dreamland.

—23rd—

Early awake and packing for the return trip with no time available for even a bit of shopping. Working on convention problems until time to appear at the College of Pharmacy of the University of California to address the student body at eleven. A round of visits to the various departments at the college with Dean Daniels. After addressing the students, to lunch at the Medical Center, meeting members of the medical staff and conversing especially with Drs. Dailey, Daniels and Eiler on the place of the pharmacist in public health education. All agreed that public health educators on pharmacy college faculties will have to be provided, and horizons will have to be expanded considerably. At 2 p. m. on the way to Oakland to visit the Navy hospital pharmacy there. Met at the hospital by Captain Broaddus, the popular C. O. of this extensive installation, and found the hospital corpsmen in the pharmacy ready for emergencies. By careful conservation of time, completed the survey and landed at the Oakland S. P. depot in time to board the streamliner "City of San Francisco" for the journey homeward.

—24th—

Riding all day in comfort and able to wade through stacks of reading matter. A pleasant two-

minute visit with Wyoming University Pharmacy College Dean O'Day while the train stopped briefly at Laramie.

—25th—

Rolled into Chicago at 10:45 a. m. as scheduled on the timetable and mentally conferred a "well done" citation upon the engineer. Telephone contacts with Dr. Hugo Hullerman of the American Hospital Association, Dean Serles, Pat Costello and others, learning with sorrow that A. PH. A. senior past president F. J. Wulling of Minnesota had passed away. At 4:30 p. m. on the last leg of the homeward trip via the B. & O.'s "Capital Limited."

—26th—

The B. & O. on time as usual and glad to get back to the capital city even though the mail and papers are piled high. In the afternoon getting some pointers from a visit to the Straus Memorial dedication where President Truman officiated and Archie Roosevelt, son of T. R., presided.

—27th—

A big day at the office after an absence of two weeks, starting with a staff meeting followed by individual staff conferences, and then a series of telephone calls to bring many activities up to date. In the afternoon to join representatives of scientific and professional societies who met with A. A. A. S. Secretary Moulton to initiate plans for the 50th anniversary meeting of this organization in 1948.

—28th—

A last-minute problem to solve with A. PH. A. election bulletin printed on too heavy stock and improperly trimmed to come within one-ounce postal rate. Long discussions on JOURNAL design and make-up for 1948. Visiting briefly with Dr. Blauch and the Pharmacognosy Committee in session in our reading room endeavoring to solve curricular problems. A similar committee handling pharmacy problems met here all last week and we are told that our library and other facilities have been of help.

—29th—

The day's routine interrupted to address G. W. University pharmacy students on opportunities which lie ahead for them.

—30th—

Now conferring with U. S. Public Health Service officials on ways and means of integrating America's pharmacies into a continuous public health information service.

J. C. McNULTY, RETIRED PHARMACIST, DIES

James Cleand McNulty, life member of the AMERICAN PHARMACEUTICAL ASSOCIATION and a retired Pittsburgh pharmacist, died on October 10. He was a graduate of Washington and Jefferson College and of the Pittsburgh College of Pharmacy. After spending some time in the commercial practice of chemistry, Mr. McNulty entered the practice of pharmacy in Pittsburgh.

A. Ph. A. Branches

AS LOCAL and student branches resumed regular sessions with the coming of fall, a trickle of meeting reports began to reach A. PH. A. headquarters. These are summarized below and will remind other branches to submit complete and regular reports, so that those carrying on the ASSOCIATION's work at the local level will receive credit in the JOURNAL. If all branches cooperate, this column will function properly as a meeting ground where A. PH. A. branches can exchange ideas for professional projects and program events.

The new ASSOCIATION year brings into full swing the programs of recently organized local branches at Albuquerque, N. M., and Milwaukee, Wis. (Albuquerque and Southeast Wisconsin Branches, respectively). During the past year charters were granted to six new student branches: University of Michigan, University of Minnesota, Drake University, Oregon State College, Idaho State College and Duquesne University. Organization of student branches is being completed at the University of Tennessee and the Medical College of South Carolina.

LOCAL BRANCHES

Members of the **New York Branch** heard an outline of the coordinated research behind a prescription product on the pharmacist's shelf at their October meeting, when Dr. J. B. Rice, vice-president and director of Medical Research, Winthrop-Stearns, spoke on "A New Professional Product Is Born."

Recent guest speakers of the **Northwestern Ohio Branch** have been Prof. Anton Hogstad, Jr., of Toledo University and Donald E. Fenstermaker of the DeVilbiss Co. The title of Prof. Hogstad's address was "Upsetting the Apple Cart." Mr. Fenstermaker discussed "Principles of Aerosol Therapy."

At an early fall meeting of the **Northern Ohio Branch,** Dr. George Rieveschl, Jr., of Parke, Davis & Co., spoke on "The Chemistry of Antihistamine Drugs."

Among the delegates at the Milwaukee convention were Serapio R. Rosado, delegate from the **Puerto Rico Branch,** and his alternate, Gilberto Hidalgo, together with other members from the "Island." A summary of the past year's activities submitted by the Branch reflects marked advances both in membership and program development. Progress was made in plans to establish a pharmacy scholarship at the University of Puerto Rico, one session featured a

discussion of the VA prescription program for veterans, and addresses on liver preparations and on the pharmaceutical industries of Puerto Rico highlighted other sessions.

STUDENT BRANCHES

New officers of the **University of Illinois Branch** worked through the summer developing bigger and better programs for the branch meetings during the current school year. A membership drive, a talent show, a dance, and a student essay contest are among the activities scheduled. A publication sponsored by the student branch, with John Fordonski as editor, will be sent to all alumni of the University's College of Pharmacy. The membership drive, under the chairmanship of Raymond J. Dauphinais, is being conducted among upper classmen as well as among freshmen. The new officers are: Paul Achenbach, president; Janet L. Corgan, vice-president; Robert C. Gustus, treasurer; and Mary E. Martin, secretary.

Acting as hosts to the freshman class on orientation day, the **University of Illinois Branch** helped show new students the "ropes" of the College. The day ended with a student-faculty dinner, followed by entertainment sponsored by branch members. Two Mallinckrodt films on ether were shown and music was provided by members of the branch. Dean Earl R. Serles addressed the group on present-day conditions in the profession.

Fordham University Branch has elected new officers for 1947–1948 as follows: Morton Roller, president; Grace Phillips, vice-president; Theresa Tyminski, secretary; and Leonard Berger, treasurer.

Members of **Southwestern Institute of Technology Branch** have been holding weekly meetings since the fall semester began. Here are the new officers elected at the first meeting: James Guy Crook, president; Kenneth Coker, vice-president; and Johnnie Anderson, secretary-treasurer. The following week, Pat Henry and John McNair of the Fox Vliet Drug Co. were guest speakers. The subject under discussion concerned competitors of pharmacy. W. D. Patterson, secretary of the Oklahoma State Board of Pharmacy, talked on the branch members' future in pharmacy, at their third meeting. A long-planned picnic was held the following evening and, on September 30, Frank Cantrill of the Owens-Illinois Glass Co. spoke and showed motion pictures on manufacture of glass and glass containers.

Secretary Sara LeMaster, **University of Mississippi Branch,** reports the following officers elected: Jack Peeples, president; Clyde Huggins, vice-president; Sara LeMaster, secretary-treasurer.

Mary Lancaster, secretary of **Howard College (Ala.) Branch,** reports that membership is on the increase through the efforts of Joe Barnett of the Membership Committee and his co-workers. During the first two weeks of the fall quarter 21 applications for membership were received. The branch welcomed Dr. C. Lee Huyck, formerly of Columbia University, as their new dean.

CHAIR IN PHARMACY HISTORY ESTABLISHED AT WISCONSIN

A full professorship in the history of pharmacy established at the University of Wisconsin is believed to be the only post of its kind in the world. Dr. George Urdang, director of the American Institute of the History of Pharmacy, has been named as the first occupant of the new chair.

The appointment was made within the frame of a unique history of science unit at the University, which also includes a professorship for the history of biological sciences, another for the history of the physical sciences, and a third post for the history of medicine.

COLLEGES NEED 99 FACULTY MEN AND 148 MORE IN THREE YEARS

Ninety-nine faculty members are currently needed by 61 of the nation's pharmacy colleges, a tabulation by the Pharmaceutical Survey revealed. Colleges also reported that 148 additional teachers of pharmacy would be needed during the next three years. The Survey group expressed concern with this situation, which the director termed "a weak link in the chain supporting the structure of professional training."

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PROPYL THIOURACIL (from p. 593)

related to thiouracil and may be considered to have a similar potential for the type of untoward reactions which led to the original warning-notice requirement.

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NAVY POSTS OPEN TO FORMER OFFICERS

QUITE a large number of permanent commissions in the Regular Navy Medical Service Corps are now available to four-year graduates of accredited pharmacy colleges who served as Navy officers during the war. With the passage of the Medical Service Corps legislation, which creates opportunities to utilize the professional abilities of pharmacists in commissioned rank, it becomes important that adequate and competent personnel be made available. Since the law requires that present openings be filled by transfer of Reserve and Temporary officers of the Navy, these opportunities should be called to the attention of pharmacists who served as officers in the Navy during the war and who may be eligible for transfer to permanent commissions in the Medical Service Corps.

The present procedure for appointments is authorized in Section 5 of Public Law 347, 79th Congress. It provides for appointment of Reserve and Temporary officers of the Navy to permanent commissioned rank in the Regular Navy. It further provides that such appointments will be open to any person who served in such officer capacity during World War II, who was separated under honorable conditions, and who meets the educational and age requirements prescribed by the President of the United States.

This provision (of P.L. 347, 79th Congress) is specifically referred to in that part of Public Law 337, 80th Congress, which established the Navy Medical Service Corps. It states (Sec. 203 of Title II) that "during the period that appointments to the Regular Navy may be made pursuant to Section 5 of the Act of April 18, 1946 (P.L. 347, 79th Cong., 2nd session), all appointments to the Medical Service Corps shall be made in accordance with the provisions of said Act." In other words, all appointments in the Navy Medical Service Corps will be by transfer of those who have served as Navy officers, until the section of the law specifying this procedure expires.

It will "expire six months after June 30 of the fiscal year following that in which the present war shall terminate or two years after the effective date of this Act, whichever shall be the later." This means that the earliest practicable date appointments in the Navy Medical Service Corps could be made from civilian life is January 1, 1949, and possibly later.

The officer transfer program applying to the Medical Corps, Dental Corps and the Medical Service Corps still remains open. (The transfer program for the Line and other Staff Corps is now closed.) There are quite a large number of vacancies at this time, according to the Navy, for appointment of officers holding a degree from a four-year course in an accredited school of pharmacy. It is believed that many graduate pharmacists who served in the Navy as officers during World War II, and who would like to make the Navy a career, are unaware of the fact that they are still eligible for transfer to permanent commissioned rank in the Navy Medical Service Corps. Regardless of the date an officer was separated from the service, he is still eligible. The only provisions to be met by these officers are the age limitations and educational and physical requirements.

Reserve or former Naval officers may make application for transfer to the Regular Navy through the nearest Office of Naval Officer Procurement, or Commandant of the Naval District.

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CARDIAC (from p. 598)

there is clearly need for more attention to its full meaning. It is one of the most useful units of dosage, for it represents the quantity of the drug with which a therapeutic procedure may be started. Clearly that amount cannot be expected to produce the therapeutic end point in all patients, because the susceptibility of patients varies. The utility of the average dose will differ from drug to drug.

Its utility in the case of any particular drug can be determined by a study of the frequency distribution curve. If the drug in question happens to be one in which the curve is fairly steep, which means that individuals do not show very wide differences in susceptibility, the average dose is extremely valuable; for in that case the average dose will exert the specific effect or something very close to it in the large majority of people. On the other hand, if the frequency distribution curve is fairly flat it indicates that there are relatively wide differences in susceptibility from individual to individual and that satisfactory effects are not likely to be obtained from the average dose.

I have pointed out how the approximate average dose is expected to behave in the case of full digitalization. That dose is based on the whole range of cardiac patients, ambulant, bed patients, those who are in moderate failure and those who are in advanced failure. Disappointments have been voiced over the fact that this dose has failed to produce the desired effects in a limited range of experiences.[16] Isn't that precisely what should be expected from any average dose? Is it to be expected that it will fit the individual case any better than any average sized hat fits any particular head?

Perhaps our experience with the average daily maintenance dose of digitalis will help to clear the point. The desired effect is to maintain a rate of 70 a minute. When this dose is given to a large group of patients for a period of four weeks the rate is rarely exactly 70 a minute for any given patient, but a result sufficiently close to that is obtained in about 70% of the group, namely a rate ranging between 60 and 90. The rest are either too tolerant and maintain rates up to 100 or faster or are so susceptible as to attain the rates of 40 or slower. That does not erase the importance of an average dose. It is still one of the most useful values in the solution of the problem of dosage.

The most useful average dose, from the clinical standpoint, is one which is likely to exert an effect close enough to the desired effect, in a high proportion of patients and with reasonable freedom from toxicity. By these criteria many drugs may fail to qualify, for individual differences in susceptibility may produce too wide a scatter. Unfortunately, few drugs have been properly explored for the true position of their average dose.

Dose for Particular Individuals.—Let us now turn from the notion of the average dose to the dose for the particular case. No one would challenge the simple statement that the optimum dose is one which produces the maximum therapeutic effect without toxic effects. It is in the method of applying this principle that all the trouble arises. Plans of dosage are too often devised without sufficient regard to the pharmacology of the agent, its rate of absorption, cumulation and persistence of action.

Quinidine.—The case of quinidine is a good example. It is the most important agent we possess for abolishing many disorders of rhythm and for preventing their recurrence. Experiments show that its maximum absorption takes about two hours, so that the peak effect may be expected at that time and that most of the effect wears off in less than twenty-four hours. We have also found in experiments on man[17] that a fixed daily dose shows cumulation for only three or four days, unlike digitalis in which a fixed daily dose may show cumulation over a period of two or three weeks. This signifies that any daily dosage level of quinidine which fails to produce the desired effect in three or four days is likely to fail to do so no matter how long it is continued.

I often encounter patients taking a small dose of quinidine for weeks on end without the slightest effect on the abnormal rhythm. The failure could have been predicted after the third or fourth day. The way of insuring success is to base the system on the facts concerning the behavior of quinidine which I have just mentioned. The method we apply in a case in which there is no urgency is to give 5 grains (0.32 Gm.) of quinidine three times daily, or 15 grains (1 Gm.) a day for four days. If the abnormal rhythm is not controlled, the dose is increased to 20 grains (1.29 Gm.) daily for four days. One continues to increase the dose by 5 grains daily every four days until a daily level is reached at which the abnormal rhythm goes or until minor toxic effects preclude its further use.

If there is great urgency, as in some cases of ventricular tachycardia, one builds the concentration more rapidly on the peak effect of each dose. In such a case we use 5 or 10 grains every two hours. The total dose in the day may be small or large, but even if large it is without

danger because the method has its own protective device, for the dose is continued only until the therapeutic effects occur or minor toxic effects necessitate interruption. By this method failures are few.

Mercurial Diuretics.—The tendency to overlook the principles of dosage which have gone far in establishing sound and effective digitalis therapy is particularly noteworthy in the current application of the mercurial diuretics in the treatment of heart failure. These materials, mercupurin, salyrgan with theophylline and mercuhydrin, represent one of the most noteworthy advances in cardiac therapy in the last twenty-five years. Unfortunately only a small part of the potentialities of these drugs is exploited, since they are commonly reserved only for cases in which there is frank edema or pulmonary rales occur.

It deserves emphasis that, in heart failure, edema may be present in the lungs and other tissues long before the usual clinical signs (rales and pitting of the legs), and that shortness of breath on effort, cough and orthopnea are usually much earlier signs. Patients with heart disease and these symptoms make up the largest group of potential beneficiaries of the mercurial diuretics. Furthermore, the common system of dosage calls for an injection not more often than once in four to seven days, with discontinuance of the drug until edema reaccumulates. It reminds one of the therapy with digitalis around the turn of the century; a course of treatment was given and repeated when signs of failure reappeared. The notion of the maintenance dose to prevent recurrence of failure is of relatively recent vintage. The very mention of a maintenance dose in the case of the mercurial diuretics sometimes gives rise to all the stir and alarm of a new idea.

As to dosage, one should note that the organic mercurials are usually eliminated completely or almost so in less than twenty-four hours. A dose may therefore be repeated every day with safety, and, indeed, in cases of advanced failure the results of the daily dose to abolish the failure, and the maintenance dose at suitable intervals to prevent its recurrence, provide us with one of the most dramatic aspects of modern cardiac therapy.[18]

Figure 5 shows how this system may be put into operation. This patient, who was in progressive failure for several years, was now in what appeared to be the very last stages; nearly moribund, gasping for breath, edema from the toes to the neck, the liver to the umbilicus, hydrothorax and ascites, cold and clammy sweat. She had received all the necessary drugs, namely digitalis and mercupurin. She was digitalized to the point of persistent vomiting. She had received several infrequent doses of mercupurin, which seemed to increase the urine output but made the symptoms worse, as a result of which it was discontinued. When she failed to rally she received the last rites. It required much persuasion to secure the privilege of subjecting this patient to a daily dose of the mercurial when doom seemed so certain. From the character of the symptoms, doom seemed no less certain in the first five days of treatment. The only encouragement came from the daily body weight. It began to decline from the very start. There was a long lag in the symptoms; they showed distinct improvement only after a loss of nearly 20 pounds (9 Kg.). When the daily dose was interrupted the improvement was halted. In seventeen days the patient was ambulant and nearly free from symptoms. She had lost about 65 pounds (29.5 Kg.) to reach her "dry weight." The method of trial and error established the maintenance dose, namely the dose which served to maintain the "dry weight." It turned out to be one dose three times a week. At the time of

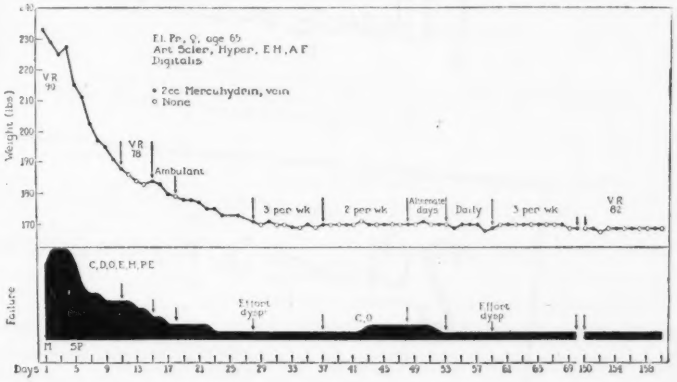

FIG. 5.—Illustration of method of producing the full effects and then establishing the maintenance dose with the mercurial diuretic in the patient with heart failure. Letters refer to symptoms (C, cough; D, dyspnea; O, orthopnea; E, edema; H, hydrothorax; P.E., pulmonary edema).

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this chart it had been in use for about four months; it is now more than a year. It is noteworthy that in the case of the mercurial diuretics an accurate chart of the body weight may be put to substantially the same use as the heart rate for the patient with auricular fibrillation treated with digitalis, or the fever chart in the case of infection treated with penicillin.

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FAIR TRADE SUPPORTED IN COURT RULING ON WAR SURPLUS ITEM

A ruling supporting fair trade laws has resulted from the first court test of applying such laws in pharmacy to the sale of war surplus stocks. The case involved a retailer, Friedman's War Surplus Center, who was selling shaving cream below the minimum resale price on the basis that the tubes were damaged. E. R. Squibb and Sons maintained that only a small number of the tubes were obviously damaged and without due notice the public would not be aware of the inferior quality of the product. The temporary injunction granted in the case was sought by the manufacturer, supported by the Washington State Pharmaceutical Association.

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[1] J.A.M.A. *135*:224 (Sept. 27) 1947.

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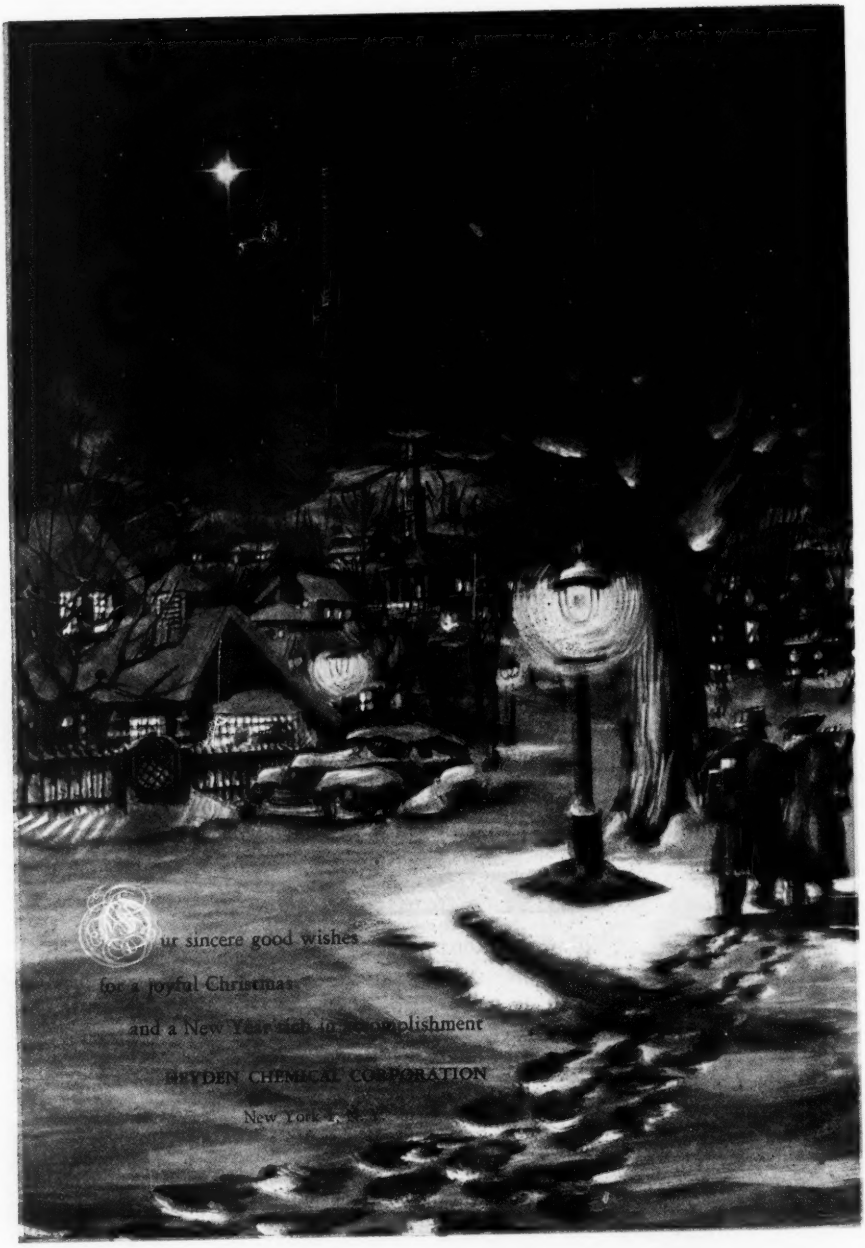
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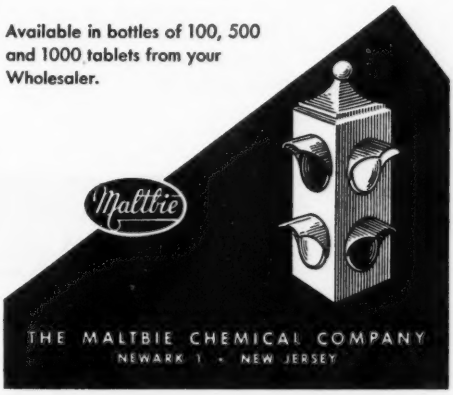

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